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# A Pediatrician's Guide to Central Precocious Puberty

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## Introduction

On the frontline of child and adolescent care, pediatricians are uniquely suited to assess signs of puberty that may signal abnormal developmental processes or underlying pathology. A working knowledge of precocious puberty diagnosis and management is, therefore, invaluable for these clinicians. Referral of children for the evaluation of precocious puberty is becoming an increasingly common phenomenon in pediatric endocrinologists' offices.[1] Although many referrals result in reassurance that the patient is within the normal spectrum of development or is experiencing benign pubertal variants, early identification and treatment is critical when true precocious puberty is present.[1,2] The need for timely attention to apparent premature development is augmented by the possibility that precocious puberty is the result of a tumor or other disorder.

Precocious puberty is defined as the onset of developmental signs of sexual maturation earlier than would be expected based on population norms. This is typically delineated as puberty onset before 8 years in girls and 9 years in boys. In its most common form, central precocious puberty (CPP), sexual maturation proceeds from a premature activation of the hypothalamic–pituitary–gonadal (HPG) axis.[3] The HPG axis is active during infancy, dormant during childhood, and reactivated at the onset of puberty. Activation of the reproductive axis is defined by a pulsatile expression of gonadotropin-releasing hormone (GnRH). This, in turn, activates the pituitary to release the gonadotropin hormones (luteinizing hormone [LH] and follicle-stimulating hormone [FSH]). Because gonadotropin hormones are the driving force for pubertal changes in CPP, the condition is also referred to as gonadotropin-dependent precocious puberty. Peripheral precocious puberty, on the other hand, is the premature sexual maturation that arises from aberrant secretion of sex steroids independent of gonadotropin production.[4] Although it does not require HPG axis activation, the presence of peripheral precocious puberty can induce HPG axis activation, resulting in CPP.[5]

## Epidemiology

The epidemiology of CPP is somewhat nebulous, with a commonly cited prevalence range of 1 in 5000 to 1 in 10 000 children.[6] CPP is known to occur more frequently in girls than in boys and has different predominant causes for each sex. Idiopathic CPP, without an identifiable predisposing condition, accounts for the majority of cases of precocious puberty in girls, but is less frequent in boys.[1,5,7] Central nervous system findings such as tumors and congenital malformations are more frequently observed in boys who present with precocious puberty.[4,5,7] It is estimated that two thirds of precocious puberty cases in boys are due to neurological abnormalities.[4] The likelihood of an organic cause for CPP is greater in patients who present at younger ages.[5,6]

Familial forms of CPP have been reported, but little is known about the pervasiveness of this condition or its underlying genetic mechanisms.[8] As pediatricians are caring for more and more children adopted from developing countries, it is also important to be aware of the greater prevalence of precocious puberty among nationally or internationally adopted children.[9-13] The reasons for this phenomenon are not well understood but are thought to be related to racial, emotional, or environmental factors such as improved nutrition or previous exposure to endocrine disruptors. The various etiologies and underlying conditions associated with CPP are presented in Table 1.

## Signs and Variants

The clinical signs of CPP are consistent with expected changes occurring during puberty, including the following:

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**Table 1.** Central Precocious Puberty Etiology[a].

| Category | Underlying Disease/Condition |
|---|---|
| Idiopathic | Sporadic |
| CNS abnormalities | Hypothalamic hamartoma |
| Tumors | Astrocytoma, craniopharingeoma, ependymoma, optical or hypothalamic glioma, LH-secreting adenoma, pinealoma, neurofibroma, dysgerminoma |
| Congenital malformations | Arachnoid cyst, suprasellar cyst, hydrocephaly, spina bifida, septum-optical dysplasia, myelomeningocele, ectopic neurohypophysis, vascular malformations |
| Acquired disease/lesion | Encephalitis, meningitis, tuberculosis, sarcoidosis granulomas, abscesses |
| Induced by medical procedures or injury | Cranial irradiation, chemotherapy, head trauma, perinatal asphyxia, CNS surgery |

Abbreviations: CNS, central nervous system; LH, luteinizing hormone.
[a]Adapted from Brito et al (2008)[4] and Carel and Leger (2008).[5]

- Increased growth velocity
- Pubic and axillary hair appearance
- Acne/oily skin
- Changes in musculature
- Body odor
- Increased appetite
- Breast or genital development

In girls, CPP often initially presents as increased growth velocity or breast development (thelarche), which may occur in isolation or associated with other physical changes, such as increased uterine volume and pubic hair development (pubarche).[4,14] The initial indicator of CPP in boys is typically an increase in testicular volume or length.[4] However, the appearance of these pubertal characteristics in a girl younger than 8 years or a boy younger than 9 years does not immediately signal CPP because there are many variants of early puberty.

In some cases, precocious puberty progresses at a slow pace or does not advance. This type of puberty variant has been described as benign or slowly progressing; affected patients have a favorable height prognosis and are thus unlikely to require treatment.[15,16] In fact, treatment with GnRH analogs, the standard of care for CPP, has not been shown to substantively increase adult height attainment in girls with slowly progressive idiopathic CPP.[16] Table 2 shows the array of clinical, physical, and hormonal characteristics that are possible differentiators between rapid and slowly progressive variants in girls. In general, the rate of progression of physical findings and the rate of progression of bone maturation are the main distinguishing factors.[5,17] Monitoring for continued evidence of advancing puberty is currently the most valuable tool available to clinicians.

There are several forms of premature development in which only a single aspect of puberty is apparent. These isolated events may be forerunners of true precocious puberty or may be self-limiting, even regressing. The likelihood of encountering these variants in clinical practice is greater than that of CPP. In a cohort of US children referred for evaluation of early puberty, 46% were diagnosed with premature adrenarche, 18% with premature thelarche, and 9% with true precocious puberty.[2] Moreover, only half of those with precocious puberty had progressive disease that required treatment.

Isolated premature thelarche refers to breast development in the absence of other clinical signs of puberty or estrogen secretion.[4] The onset of isolated premature thelarche is generally within the first 3 years of life and may continue through puberty or regress over time. In a recent study of an unselected population of girls in the United States aged 12 to 48 months, premature thelarche was present in 15 of 318 (4.7%) children.[21] At the time of follow-up (6 months or more after the initial visit), breast development was still evident in just 44% of cases. There does not appear to be adverse sequelae associated with isolated premature thelarche; bone age and growth velocity are generally unaffected.[4,22] When thelarche is the lone sign of puberty onset and is not followed by progress in other secondary sexual characteristics, the condition is considered a natural pubertal variant that does not require further treatment[23]; however, routine follow-up with measurement of gonadotropin and estradiol levels, growth velocity, and bone age is suggested. Pelvic ultrasonography may prove useful at early stages to distinguish between the isolated and progressive forms of thelarche.[4]

Premature pubarche is a common manifestation of adrenarche (a pubertal stage marked by increased adrenal androgen secretion) and is, therefore, alternately referred to as premature adrenarche in the scientific and clinical literature. Affected children may demonstrate some evidence of increased growth velocity or advanced

**Table 2.** Criteria for Differentiating Progressive From Nonprogressive Forms of Precocious Puberty in Girls[a,b].

| Criterion | Progressive Central Precocious Puberty | Nonprogressive Precocious Puberty |
|---|---|---|
| Clinical | | |
| Progression through pubertal stages | Progression from one stage to the next in 3 to 6 months | Stabilization or regression of pubertal signs or progression from one stage to the next over at least a year |
| Growth velocity | Accelerated (in excess of 6 cm per year) | Usually normal for age |
| Bone age | Usually advancing by more than 1 year per year | Not accelerating in degree of advance |
| Predicted adult height | Below target height range or declining on serial determinations | Within target height range |
| Uterine development | | |
| Pelvic ultrasonography scan[c] | Uterine volume >2.0 mL or length >34 mm; pear-shaped uterus, endometrial thickening (endometrial echo) | Uterine volume ≤2.0 mL or length ≤34 mm; prepubertal, tubular-shaped uterus |
| Hormone levels | | |
| Estradiol | Usually measurable estradiol level with advancing pubertal development | Estradiol not detectable or close to the detection limit |
| LH peak after GnRH or GnRH agonist test[d] | In the pubertal range | In the prepubertal range |

Abbreviations: LH, luteinizing hormone; GnRH, gonadotropin-releasing hormone.
[a]These criteria were developed to distinguish progressive CPP (characterized by a sustained activation of the gonadotropic axis) from nonprogressive precocious puberty (in which the gonadotropic axis is not activated) and were obtained in cross-sectional and small longitudinal studies; their reliability has not been fully evaluated.[18-20]
[b]Reprinted with permission from Carel and Leger (2008).[5]
[c]Pelvic ultrasonography is used much more frequently in Europe than in the United States. Uterine development reflects sustained exposure to estrogens and is a marker of progressive puberty.
[d]GnRH is not available in the United States for use in testing.

bone age as well as the appearance of axillary hair, body odor, and acne.[4] Pubarche and advanced growth velocity/bone age without evidence of breast development in girls or in conjunction with a prepubertal testicular volume in boys may indicate an adrenal disorder or androgen exposure.[5,23] Putative risk factors for premature pubarche include children who were born prematurely, children who were small for their gestational age, and children who are overweight or obese.[24,25] Overt puberty in children with premature pubarche generally begins early but within the normal range for the general population; adult height is not compromised.[25,26] However, premature adrenarche can be the first sign of precocious puberty and has been linked to an increased risk for patients to develop polycystic ovary syndrome and/or characteristics of metabolic syndrome, including obesity and type 2 diabetes mellitus.[26]

Isolated premature menarche is defined as vaginal bleeding occurring prior to age 8 and without accompanying signs of puberty. There may or may not be elevation in gonadotropin or estradiol levels.[4] Girls presenting with premature menarche should be assessed via physical examination and medical history to eliminate the possibility that vaginal bleeding was caused by genital injury, foreign body, or manipulation. Premature menarche is not considered among normal puberty variants; affected children should be evaluated for possible ovarian or uterine pathology.[23]

## Diagnosis

The first step in the diagnosis of precocious puberty is to obtain a detailed family and personal history. Special attention should be given to the following:

- Order and timing of secondary sex characteristic appearance
- Age of puberty onset in parents and siblings
- Neurologic signs and symptoms
- Past exposure to estrogen, androgen, or mimetic compounds (including over-the-counter products such as lavender and tea tree oils[27])

The growth chart can determine the patient's pace of growth, comparing the height and weight velocity against standard growth curves. If past data are not available, growth velocity will need to be monitored prospectively for 3 to 6 months or more.[23] Most girls with CPP track above the 75th percentile in growth velocity. Because boys have their growth spurt later,

advanced growth velocity is not necessarily detected at early stages of CPP.

Physical examination should include assessment of Tanner staging and signs of puberty. Early signs of precocious puberty may be subtle, particularly in girls. Staging of breast development is particularly challenging in overweight or obese girls[28]; careful palpation can help distinguish glandular breast tissue from adipose tissue, which is softer and more diffuse compared with a true breast bud. Genital development staging in boys can be determined visually, but this method is subject to a higher degree of interrater variability compared with objective measure of testicular volume using an orchidometer.[29] If an orchidometer is not available, testicular volume can be estimated using the formula 0.71 × length × width × height.[30] Testicular volume >4 mL (roughly larger than a black olive) or length of >2.5 cm is indicative of pubertal development, except in boys younger than 2 years for whom testicular volume may not have appreciably increased despite the onset of precocious puberty.[4] Testicular size may also remain prepubertal in boys with adrenal disorders, premature pubarche, or peripheral precocious puberty caused by conditions other than testicular disorders.[5] Testicular ultrasonography is recommended in cases of asymmetric testicular size or when peripheral precocious puberty is suspected.

When the above signs point to precocious puberty, the next step in diagnosis and follow-up would be to obtain a radiograph of the left hand to determine bone age. In patients with CPP, bone age is advanced relative to chronological age. Bone age greater than 2 standard deviations above the normal range for a child's chronological age is characteristic of rapidly progressing precocious puberty.[31] The degree of bone maturation may be less pronounced if precocious puberty is detected early (ie, not much time passed since onset of puberty and, therefore, the bone age is not yet advanced). If a slow progressing variant of CPP is suspected, repeated bone age assessment before initiation of therapy may be warranted, as these patients typically achieve normal adult height without treatment.[31] Notably, all methods of assessment have bias, and thus, bone age X-ray reading remains an inaccurate tool at best.[3]

Once a bone age has been obtained, it can be used to estimate a patient's predicted adult height. By comparing the predicted adult height with the target height calculated from parent's height measurements,[18] the magnitude of loss in height potential can be evaluated.

Measurement of hormone levels helps in the differential diagnosis of precocious puberty (Figures 1 and 2). Initial workup in the outpatient pediatrician's office should include assessment of basal LH and FSH levels. Observation of basal elevations in LH by sensitive assays may be sufficient to diagnose CPP without the need for GnRH challenge[4,32,33]; however, LH response to GnRH is the "gold standard" for CPP evaluation. The GnRH stimulation test is performed by administering exogenous GnRH or a GnRH analog and obtaining blood samples at baseline and at regular intervals thereafter. Peak serum LH values above a certain assay-specific threshold signify CPP.

Morning plasma testosterone levels in the pubertal range are indicative of precocious puberty in boys but are not present in all cases.[4,5] Similarly, low levels of estradiol do not rule out a CPP diagnosis because many girls with precocious puberty have estradiol levels in the prepubertal range.[4] Excessively high estradiol levels (>100 pg/mL) may be concerning as a potential indicator of ovarian cysts or tumors.[5] The evaluation of other hormone levels will depend on the clinical case at hand. For example, thyroid-stimulating hormone and thyroxin levels should be measured if hypothyroidism is suspected. In boys with early signs of puberty accompanied by advanced growth velocity and bone age but a prepubertal testicular volume, concentrations of adrenal steroid precursors (particularly 17-hydroxyprogesterone) should be measured.

For all hormonal measurements, it is important to use sensitive assays that have been validated in a pediatric population. Also, as there is natural variation in hormone levels during childhood, reference standards should be specific to the age of the patient in question. Consultation with a local endocrinologist may be helpful in guiding laboratory and assay selection. As of this writing, there are 2 primary pediatric endocrine commercial laboratories: Esoterix (Austin, TX), a subsidiary of Labcorp (Burlington, NC), and Nichols Institute (San Juan Capistrano, CA), now owned by Quest Diagnostics (Madison, NJ).

Use of magnetic resonance imaging (MRI) of the head for the identification of central nervous system lesions in boys and girls younger than 6 years presenting with CPP is a generally accepted principle.[34] For girls aged 6 to 8 years, universal application of head MRI is debatable; critics cite a low risk of unsuspected intracranial pathology in this population. However, a recent systematic evaluation of MRI results in girls with CPP reported that pathological findings on MRI were not uncommon in girls aged 6 years and older.[35] That study's investigators concluded that head MRI should continue to be conducted as part of the assessment for girls presenting with CPP who are aged younger than 8 years. Given that intracranial pathology is more common in boys than in girls, MRI is warranted in all boys presenting with CPP.

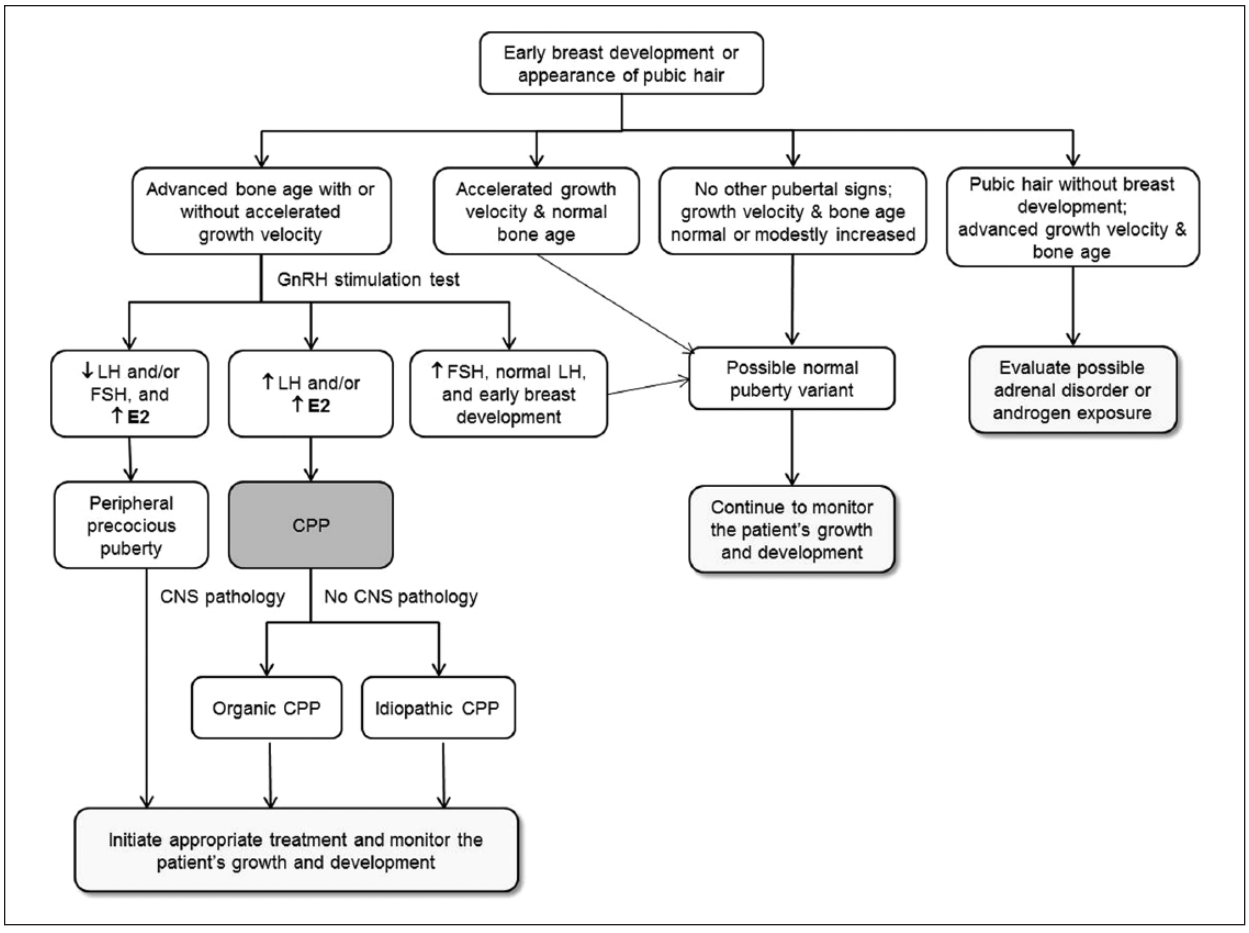


**Figure 1.** Differential diagnosis of precocious puberty in girls.
Abbreviations: GnRH, gonadotropin-releasing hormone; LH, luteinizing hormone; FSH, follicle-stimulating hormone; E2, estradiol; CPP, central precocious puberty; CNS, central nervous system.
Adapted from Sultan et al (2012)[22] and Berberoğlu (2009).[23]

The majority of preliminary patient evaluations are within the purview of the pediatrician (Figure 3). Whether advanced assessments (eg, bone age measurement, pelvic or testicular ultrasonography, etc) are performed by the pediatrician depends on the comfort level of the clinician. Referral to a pediatric endocrinologist for diagnostic evaluation and initiation of therapy is recommended when the clinician feels the evidence is consistent with precocious puberty or if there is diagnostic uncertainty. As early treatment yields the best outcomes, timely referral is essential.

## *Case Studies*

*Case 1*. A 6-year-old African American girl presents with breast buds and sparse transitional pubic hair. She is at the 95% percentile for height; bone age measurement reveals an advancement of 18 months relative to her chronological age. The patient's predicted height is consistent with that of her mother. What would be the next step for evaluating this patient?

This patient demonstrates characteristics consistent with premature pubertal development, including early stages of breast and pubic hair development and bone age advancement; however, the lack of overt impact on predicted height and modest sexual maturation may indicate a normal pubertal variant. A propensity for earlier puberty onset in African American girls compared with other racial/ethnic groups also bears consideration in this case.[36,37] The patient should be monitored closely by the clinician and her parents for evidence of further pubertal development, with repeat examination including bone age assessment in 6 months.

*Case 2*. A 7-year-old Caucasian girl presents with stage 3 breast and pubic hair development. She is currently at

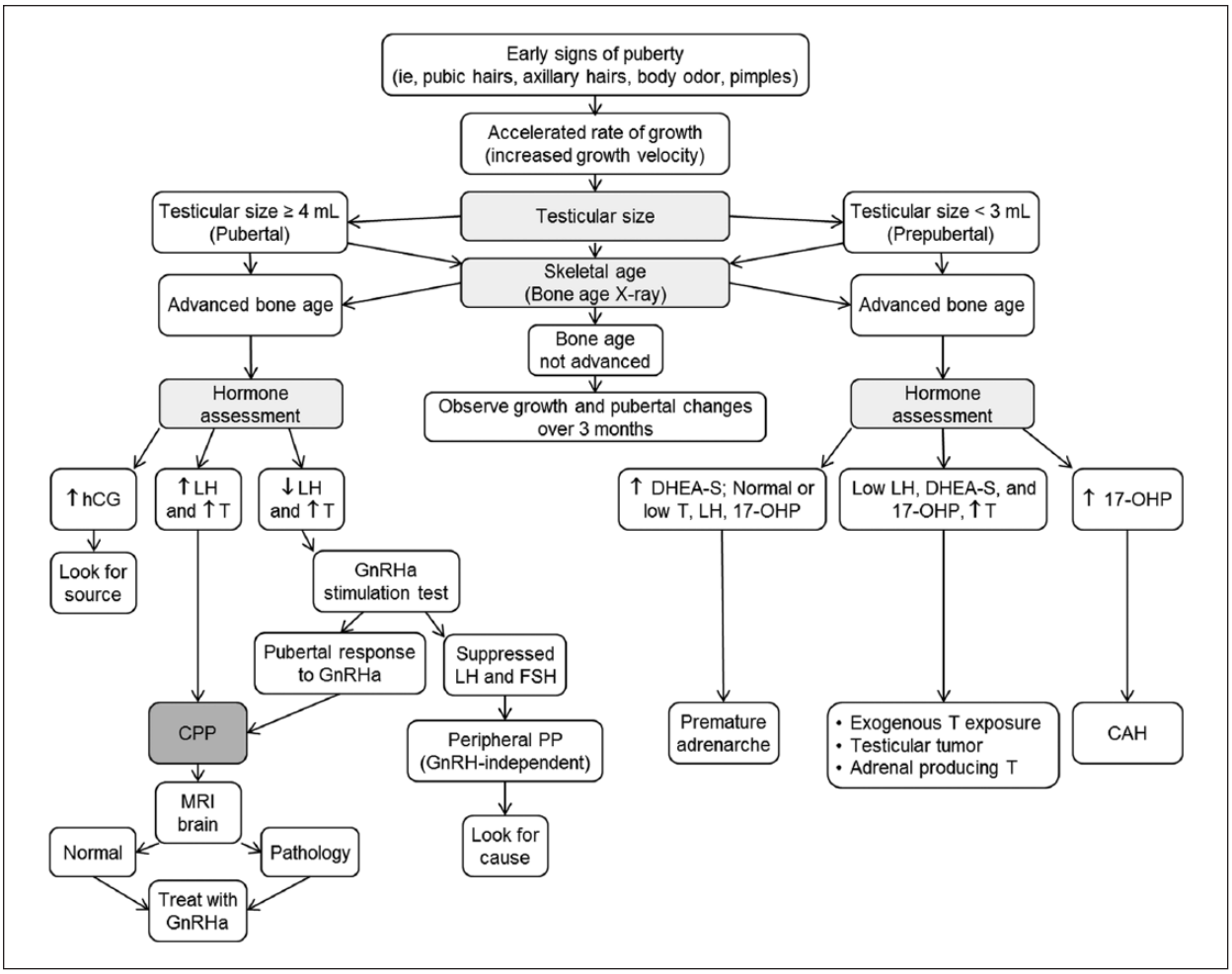


**Figure 2.** Differential diagnosis of precocious puberty in boys.
Abbreviations: hCG, human chorionic gonadotropin; LH, luteinizing hormone; T, testosterone; DHEA-S, dehydroepiandrosterone sulfate; 17 OHP, 17-hydroxyprogesterone; GnRHa, gonadotropin-releasing hormone agonist; CPP, central precocious puberty; MRI, magnetic resonance imaging; PP, precocious puberty; CAH, congenital adrenal hyperplasia.
Adapted from Carel and Leger (2008)[5] and Berberoğlu (2009).[23]

the 50% percentile for height, but was at the 25% percentile 1 year ago. Both parents are in the 25% percentile range for height. The patient's bone age is advanced by 2 years relative to her chronological age. What would be the next step for evaluating this patient?

The degree of pubertal development and obvious signs of both growth acceleration and bone age advancement are indicative of precocious puberty. This patient should be referred to a pediatric endocrinologist for further evaluation.

*Case 3.* At an annual well-child visit, the adoptive parents of a 6-year-old girl report a rapid rate of growth and the presence of body odor but no other visible signs of puberty. Physical examination reveals that the child has an above normal body mass index, but Tanner stages of development are prepubertal. Bone age is slightly advanced relative to the child's chronological age. What would be the next step for evaluating this patient?

In this case, the clinical presentation is consistent with either CPP or premature adrenarche. As an adopted child, the chances of a precocious puberty finding are elevated relative to the general population.[11,12] Nonetheless, careful attention should be paid to possible sources of previous or current androgen exposure. Elevated body weight is another risk factor for early puberty onset that should be taken in account for this case.[28,38] In addition to close monitoring for signs of continued pubertal development, the clinician should discuss with the patient's family the potential impact of excess weight on puberty onset and give guidance on weight management strategies.

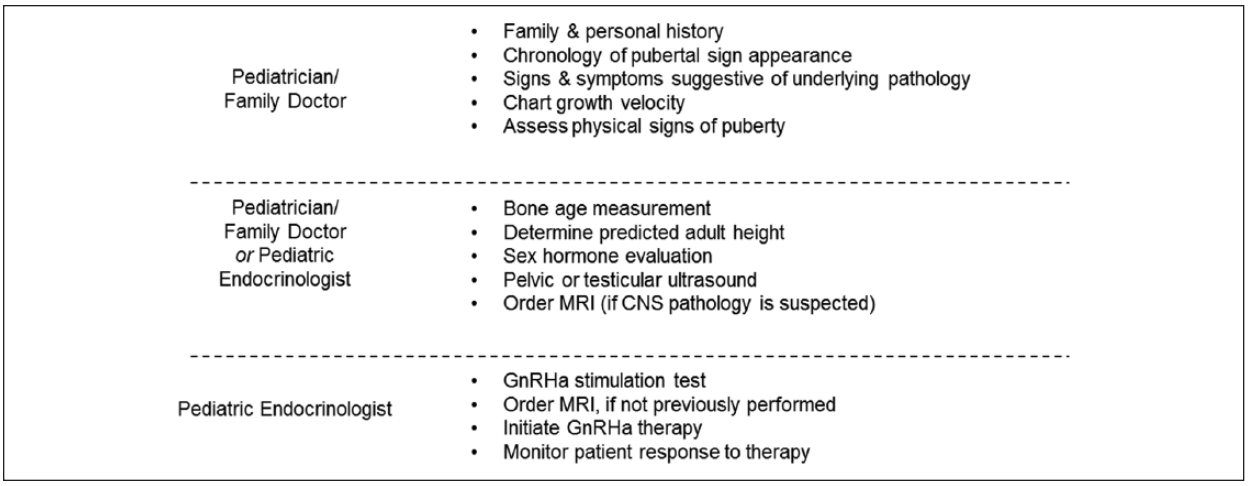


**Figure 3.** Diagnostic assessments in children with suspected precocious puberty.
Abbreviations: MRI, magnetic resonance imaging; CNS, central nervous system; GnRHa, gonadotropin-releasing hormone analog.

## Treatment

One of the driving forces for treating CPP is to promote satisfactory adult height gains in patients with the disease. Historical data from untreated patients with precocious puberty indicate a height loss of approximately 20 cm (7.9 in.) for boys and 10 cm (3.9 in.) for girls.[15] The potential psychosocial consequences of developing ahead of one's peers are also a consideration when determining whether to suspend pubertal development. Early maturation, even within the normal spectrum of developmental timing, heightens social anxiety among girls.[39] In both girls and boys, earlier puberty onset is associated with increased likelihood to engage in sexual risk taking, substance abuse, and antisocial behavior.[40,41] A concern that has more recently emerged is the putative link between early menarche or male puberty and gynecological, breast, or testicular cancer.[26,42]

The standard of care for suppression of pubertal development in patients with progressive CPP is GnRH analog therapy.[34] GnRH analogs mask the pulsatile endogenous GnRH release, which thereby causes a decrease in LH and FSH synthesis. There are several GnRH analogs available in the United States, which differ in terms of duration of action, dosing schedule, and route of administration (Table 3). All of the available agents have proven efficacious for HPG axis suppression, yet long-acting formulations are generally preferred to short-acting formulations because of the potential for improved patient compliance.[34] One of the more recent developments among the long-acting formulations is the once-yearly subcutaneous histrelin acetate implant. This thin, flexible tube is placed under the skin in the upper arm via a small incision, where the implant remains for 12 months before removal. Other depot preparations are administered as intramuscular injections monthly or every 3 months.

The 2009 consensus statement on the use of GnRH analogs in children states that the best outcomes with GnRH analog therapy in terms of height gains for girls are achieved when progressive CPP onset is apparent before age 6 years.[34] For those girls who present at age 6 years or older, the decision to initiate treatment depends on each individual case. It is recommended that all boys with progressive CPP and compromised adult height potential receive treatment. As mentioned previously, patients with slow progressive forms of CPP may not require treatment. Consequently, before initiating therapy, a period of follow-up is advisable to ensure that the observed precocious puberty is progressive.

Pubertal development resumes after discontinuation of GnRH analog therapy.[34] No adverse effects on reproductive development or fertility have been found to be associated with GnRH agonist therapy for the treatment of CPP. Potential concerns, including enduring effects on bone mineral density, increases in body mass index, and elevated risk for polycystic ovary syndrome, appear to be unfounded.

Whether or not they receive treatment, patients with CPP require routine monitoring to detect signs of pubertal progression. Growth velocity and bone age should be evaluated every 6 months. Continued advancement of CPP despite therapy may indicate an issue with treatment compliance. Pediatricians and endocrinologists should work in concert to ensure that the patient is monitored both in the clinic and at home. An established relationship and regular contact between families and pediatricians opens the lines of communication, allowing the

**Table 3.** Characteristics of Gonadotropin-Releasing Hormone Agonist Analogs Available in the United States That Are Used in the Treatment of Central Precocious Puberty[a].

| | Rapid Acting | Monthly Depot | 3-Month Depot | 12-Month Implant |
|---|---|---|---|---|
| Agent | Nafarelin | Leuprolide | Leuprolide | Histrelin |
| Brand name[b] | Synarel | Lupron depot-PED-1 month | Lupron depot-PED-3 month | Supprelin LA |
| Dosing | 3-4 times daily (intranasal) or once daily (subcutaneous) | Every 28 days | Every 90 days | Every year |
| Peak serum concentrations | 10-45 minutes | 4 hours | 4-8 hours | 1 month |
| Onset of therapeutic suppression | 2-4 weeks | 1 month | 1 month | 1 month |
| Advantage | Quick onset/offset of effect | Dosing and efficacy well studied | Fewer injections and fewer compliance concerns | No injections needed; noncompliance potentially less concerning |
| Disadvantage | Multiple daily doses needed; requires compliance with daily administration | Painful injections; requires compliance with monthly injections | Painful injection | Requires a minor surgical procedure for insertion and removal, which may require general anesthesia |
| Side effects and cautions | Generally reserved for patients with sterile abscesses from depot injections | Pain, erythema, inflammatory reactions, and sterile abscesses at the injection site | | Implant site reactions, potential scarring |

[a]Adapted from Carel and Leger (2008)[5] and Carel et al (2009).[34]
[b]Synarel is manufactured by G. D. Searle LLC, New York, NY.[19] Lupron depot-PED-1 month and Lupron depot-PED-3 month are manufactured by AbbVie Inc, North Chicago, IL.[20] Supprelin LA is manufactured by Endo Pharmaceuticals, Inc, Malvern, PA.[43]

pediatrician to address concerns and educate parents regarding changes to be aware of in their child. Parental vigilance in observing and reporting signs of further pubertal development should be encouraged.

## Clinical Insights

In contemporary clinical practice, multiple factors can make it challenging to delineate CPP from early normal puberty variants. There appears to be a population-wide decrease in the age of puberty onset, in addition to some underlying racial/ethnic differences in puberty chronology.[37,38] Speculation abounds as to the root of large-scale changes in puberty onset, with suspected factors including the obesity epidemic that plagues many Western nations and possible environmental exposure to endocrine disrupters, particularly in developing countries.[9,28,38] Based on epidemiologic data available at the time, in 1999, the Lawson Wilkins Pediatric Endocrine Society published a statement recommending that the age limits for evaluating precocious puberty in girls presenting with breast development or pubic hair be pushed back to before age 7 in white girls and age 6 in African American girls. Exceptions to this would include cases of unusually rapid progression, the presence of neurologic pathology, or when puberty progression causes extreme emotional distress for the patient or family.[36] This guidance is controversial and has the potential to overlook patients who could benefit from therapeutic intervention. Pediatric endocrinologists in the United States have, by and large, held with the traditional recommendations for evaluating precocious puberty when signs present before age 8 in girls and age 9 in boys.[5]

Early sexual maturation and/or the diagnosis of precocious puberty can be a scary proposition for parents and children alike. From the perspective of the pediatrician, this is a teachable moment to address gaps in knowledge, misconceptions, or concerns the family may have regarding puberty. Lay perceptions of what constitutes "normal" development may not be consistent with medical precepts and are subject to cultural and family influences. Pediatricians are in a position to reassure parents that although puberty onset occurs at an average age of 10.5 years for girls and 11.5 years for boys, it can range from 8 to 13 years for girls and 9 to 14 years for boys. Menarche, which occurs on average at age 12.5 years, is a common subject of anxiety for parents. Parents are often concerned that growth will stop at the time of menarche, when, in reality, girls will continue to grow an average of 2 additional inches. Parents also worry that menarche will follow rapidly after breast development, yet there is generally a 2-year delay

between these developmental milestones (although this may be foreshortened in patients with CPP). The physical examination conducted before a child's entry into kindergarten would be an important opportunity for this type of discussion with parents. By the time children reach school age, they require less supervision in dressing and bathing, which may result in parents being unaware of physical changes already taking place unless they are attentive to indicators of early development. Early dialogue about puberty may also allow pediatricians to combat the perception that the increased height or physical changes associated with precocious puberty are good, rather than worrisome—a belief that causes some parents to feel disinterested in further evaluation and follow-up for their child.

Time should also be spent assessing how a child perceives his or her development, especially in reference to their peers and what they hear from family members. Along with the physical aspects of puberty, it is important to assess for the emotional implications of early puberty. Children who appear older may oftentimes be pressured by their family or social circles to act more mature than their age. The pediatrician has the opportunity to address issues regarding a child's self-image, anxiety or mood changes, sexuality, and peer influences. Even when findings are reassuring and point to a normal variant in development, a child still benefits from guidance during this stage in life when social influence and peer pressure can be especially challenging and harsh.

It is important to listen to the child's questions and watch for nonverbal cues, like tears and fear. Even phrases like "Your body is growing up a little too soon" can make a child feel like something is "wrong" with them. They need to be told that they are not going to die, they did not do anything wrong, and they will have a normal life. Parents often ask questions about how to talk to their child about sex, masturbation, coping with dressing age appropriately, and whether they should allow their young child to use deodorant. Some parents appreciate permission to cut pubic hairs or shave axillary hairs, and even counseling on sports bra options can be reassuring. Once a child is on treatment, parental concerns focus on future fertility.[44-47]

Even after having seen the endocrinologist, some families and children benefit from ongoing conversations with their primary care provider to help process information over time. Common parental questions/concerns that the pediatrician may need to address include the following:

- Will treatment and follow-up return the patient to the prepubertal state or simply stop the progression of puberty
- How to talk to their child about the condition
- What to tell friends and relatives
- The effect of precocious puberty on their child
- How tall will their child be
- Long-term risks of treatment
- Fear that the child is not mentally prepared to handle menses or will lose her innocence and become more like a teenager
- Types of child and family support that are available

Where there are issues of poor acculturation or health literacy within the family, information from reliable external sources can be limited. Providing accurate, easily understood, and culturally appropriate education is important in allaying parental fears and helping children adapt to the physical and emotional changes they are experiencing.

## Conclusions

CPP is a manageable disease for which there are effective treatment options when the condition is identified early and treated appropriately. As the primary source of health care provider interaction for children, pediatricians are ideally situated to be the first to detect signs of precocious puberty through direct observation and proactive discussion with patients and their families. Pediatricians should carefully evaluate growth charts and perform pubertal examinations at all well-child visits. Routine visits also give clinicians occasion to query parents about their child's development or if they have observed moodiness, acne, or other signs of puberty in their child. Physical clues and diagnostic evaluations create an overall clinical picture that allows the clinician to distinguish normal puberty variants from CPP. Prompt referral to a pediatric endocrinologist gives the patient with CPP the best chance to benefit from therapeutic intervention. Ongoing follow-up is necessary to monitor the child's development and provides further opportunities for the pediatrician to address psychosocial issues that may arise.

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