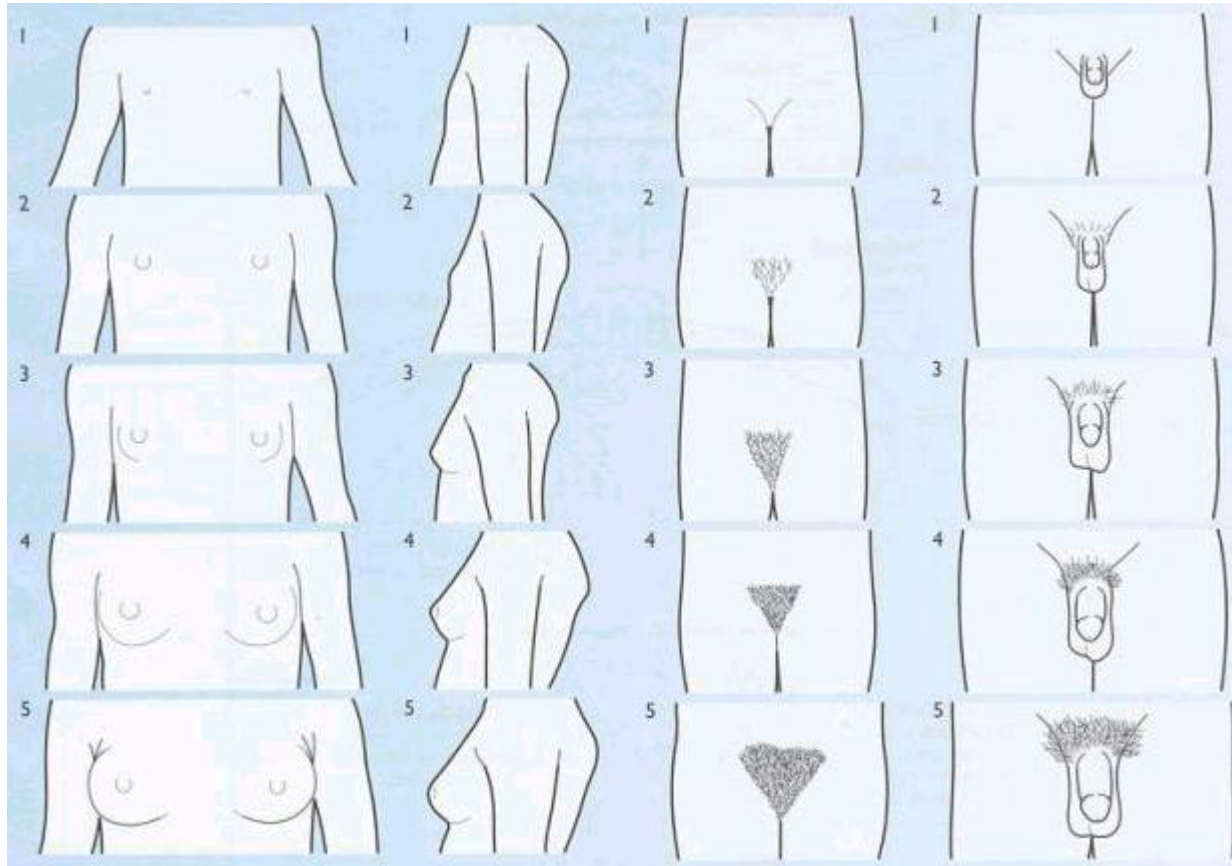


Tanner Staging





Tanner Staging

- Pubic Hair
- Stage 1: Prepubertal (can see velus hair similar to abdominal wall)
- Stage 2: Sparse growth of long, slightly pigmented hair, straight or curled, at base of penis or along labia
- Stage 3: Darker, coarser and more curled hair, spreading sparsely over junction of pubes
- Stage 4: Hair adult in type, but covering smaller area than in adult, no spread to medial surface of thighs
- Stage 5: Adult in type and quantity, with horizontal distribution



Tanner Staging

- Development of external genitalia
- Stage 1: Prepubertal
- Stage 2: Enlargement of scrotum and testes, scrotum skin reddens and changes in texture
- Stage 3: Enlargement of penis (length at first), further growth of testes
- Stage 4: Increased size of penis with growth in breadth and development of glans, testes and scrotum larger, scrotum skin darker
- Stage 5: Adult genitalia



Tanner Staging

- Breast development
- Stage 1: Prepubertal
- Stage 2: Breast bud stage with elevation of breast and papilla, enlargement of areola
- Stage 3: Further enlargement of breast and areola, no separation of their contour
- Stage 4: Areola and papilla form a secondary mound about level of breast
- Stage 5: Mature stage, projection of papilla only, related to recession of areola



Precocious Puberty

Morning Report

April 10, 2006

Monica Tranetzki



Puberty

- Development of secondary sexual characteristics
- Gonadarche
- Adrenarche



Puberty

- Girls

- Breast development, can be unilateral
- Pubic and axillary hair
- Menses 2-3 years after breast development starts
- Growth spurt early in puberty, usually appears by time of initial evaluation



Puberty

- Boys

- Testicular enlargement, usually unnoticed
- About 1 year after, growth of penis and scrotum, with appearance of pubic hair
- Growth spurt later than in female puberty, but often starts by the time other physical changes are noted



Precocious puberty

- Development of secondary sexual characteristics before 8 years old in girls, 9 years old in boys
- In US, incidence is 1 per 5,000-10,000 individuals



Precocious puberty

- Etiology:
 - Central (GnRH dependent): early but otherwise normal activation of hypothalamic-pituitary-gonadal function (always isosexual)
 - GnRH and gonadotropin independent: autonomous excess peripheral secretion of sex steroids (can be iso- or contrasexual)
 - Incomplete: early development of secondary sexual characteristics and is a variant of normal puberty



Central precocious puberty

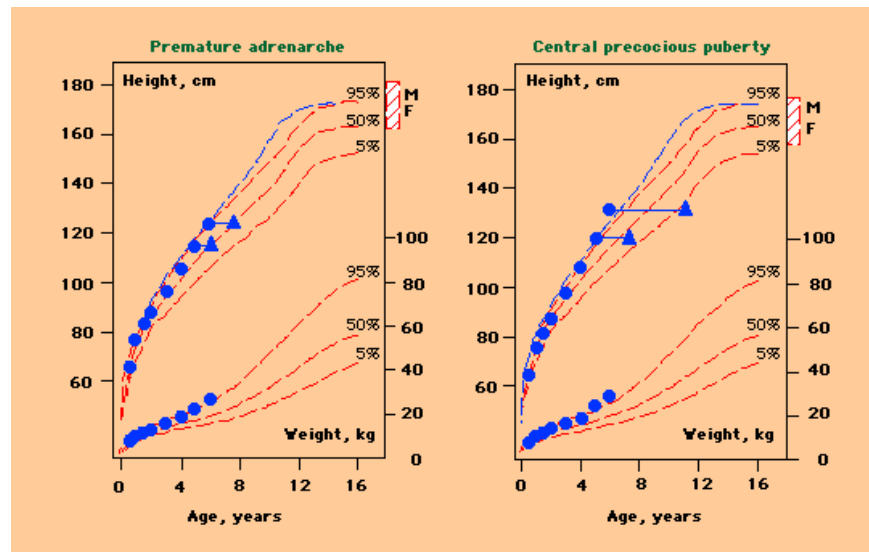
- Epidemiology
 - 5-20xs more common in girls
 - 80-90% are idiopathic
 - Idiopathic CPP is 8xs more common in girls



Central precocious puberty

- Morbidity
 - Psychosocial stressor
 - Short stature: increase in sex steroids causes increase in height velocity and rate of skeletal maturation, leading to premature epiphyseal fusion, causing paradox of short adult stature despite being tall childhood stature

Central precocious puberty



Growth patterns in the assessment of precocious puberty in girls Height (upper curves) and weight (lower curves) plotted versus age against the backdrop of normal expectations for growth. The triangles reflect height versus bone age, and the shaded box on right hand y axis represents the 95 percent confidence limits for adult height based on parents' heights: M = mother's height centile; F = father's height centile). In the left panel, a child with premature adrenarche has had a modest acceleration of linear growth and skeletal maturation consistent with the impact of relatively weak adrenal androgens. Her "height age" and bone age are equal (both approximately a year in advance of chronological age). In the right panel, the more dramatic impact of gonadal steroid production is evident in a girl with central precocious puberty. The linear growth rate is more accelerated and the skeletal maturation dramatically advanced (bone age >> height age > chronological age).



Central precocious puberty

- Etiology
 - Idiopathic
 - CNS tumors
 - Most common: Hamartomas of the tuber cinereum, they contain GnRH neurons and act as ectopic hypothalamic tissues, also can present as laughing seizures
 - Also: astrocytomas, ependymomas, pineal tumors, optic gliomas (NF 1), hypothalamic gliomas
 - Acquired CNS injury: inflammation, surgery, trauma, radiation therapy, abscess
 - Congenital anomalies: hydrocephalus, arachnoid cysts, suprasellar cysts, midline defects
- CNS abnormalities interrupt the central pathways that suppress the onset of puberty

Central precocious puberty

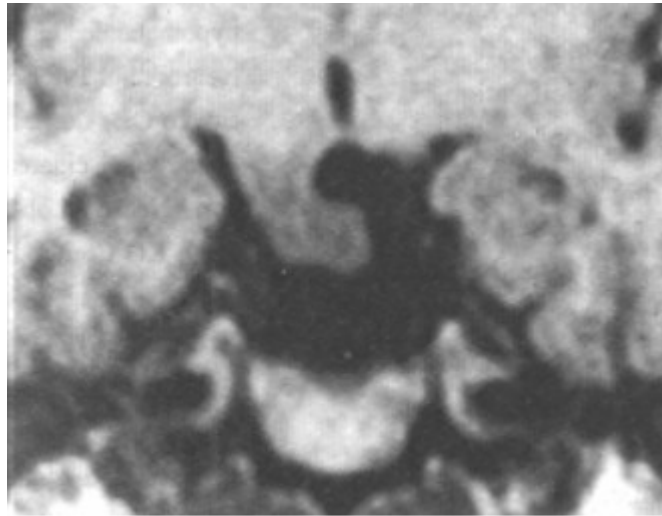


Figure 2: Coronal T1WI MR image shows a small rounded hypothalamic mass projecting into the suprasellar cistern.



Central precocious puberty

- Most commonly idiopathic, but great association with CNS causes
- Younger the child greater the chance of finding CNS pathology
- Boys younger than 9 years old, incidence of CNS findings is greater than in girls



GnRH independent precocious puberty

- Less common than CPP
- Numerous etiologies
- Circulating sex steroids cause secondary sexual development, which come from either the adrenal gland or the gonad, independent of the hypothalamic-pituitary portion of the pubertal axis



GnRH independent precocious puberty

- Morbidity
 - Similar to CPP:
 - Psychosocial stressors
 - Short adult stature
 - Also depends on etiology



GnRH independent precocious puberty

Etiologies:

■ Girls:

■ Ovarian cysts

- Follicular cysts most common cause of GnRH independent precocity in girls, often present after episode of vaginal bleeding

■ Ovarian tumors

- Rare
- Granulosa cell tumors and gonadoblastoma



GnRH independent precocious puberty

- Boys:
 - Leydig cell tumor
 - Asymmetric testicular enlargement
 - Secretes testosterone
 - hCG secreting germ cell tumors
 - Secretes hCG → activates LH receptors on Leydig cells → testosterone
 - Liver tumors (hepatomas and hepatoblastomas) and choriocarcinomas of gonads, mediastinum, retroperitoneum and pineal gland
 - Familial gonadotropin-independent sexual precocity (testotoxicosis)
 - Autosomal dominant
 - Mutation on the LH receptor gene → premature Leydig cell maturation and secretion of testosterone
 - Girls not affected because need both FSH and LH for estrogen synthesis



GnRH and gonadotropin independent precocious puberty

- Both sexes:
 - Pituitary gonadotropin-secreting tumors
 - Rare
 - Elevated FSH and/or LH levels
 - Exogenous estrogen or androgens
 - Due to creams, ointments, hormonal contraceptives, anabolic steroids, placental extracts
 - Adrenal pathology
 - Adrenal tumors
 - Enzymatic defects in adrenal steroid biosynthesis (Congenital adrenal hyperplasia—most common 21 hydroxylase deficiency)
 - Boys with adrenal causes will not have testicular enlargement



GnRH independent precocious puberty

- Both sexes (continued):
 - Primary hypothyroidism (van Wyk-Grumbach Syndrome)
 - TSH is similar in structure to LH and binds to LH receptors
 - Leads to growth arrest
 - McCune Albright syndrome
 - Triad: Precocious puberty, café au lait spots, fibrous dysplasia of bones
 - Mutation of G3 protein that activates adenylate cyclase → continuous stimulation of endocrine function (precocious puberty, acromegaly, Cushings...)
 - Girls may have recurrent formation of follicular cysts



Incomplete Precocious Puberty

- Early development of secondary sexual characteristics, variant of normal puberty
 - Premature thelarche
 - Isolated breast development in girls, usually less than 3 years old
 - Breast tissue increases minimally over time, can even decrease
 - Lack of thickening and pigmentation of the nipple and areola
 - Premature adrenarche
 - Isolated pubic hair development in girls and boys, usually less than 7-8 years old
 - Due to earlier than usual increase in secretion of androgens by adrenal glands
 - Risk factor for PCOS
- Normal bone age
- Normal growth rate
- Requires close monitoring as a significant number (up to 18% of girls with premature thelarche, and up to 20% of girls with premature adrenarche) will go on to develop central precocious puberty



Initial evaluation

- Medical history
 - When were initial pubertal changes noted
 - When were pubertal changes for parents, siblings
 - Evidence of linear growth acceleration (growth charts)
 - CNS risk factors: infections, surgery, radiation therapy, neoplasm, trauma
 - Headaches, visual changes
 - History of seizures
 - History of exposure to exogenous estrogens or androgens
 - Family history of any genetic disorders: Testotoxicosis, NF Type 1



Initial evaluation

- Physical examination
 - Height, weight and height velocity (cm/yr)
 - Abnormal vital signs
 - Fundoscopic exam
 - Visual fields
 - Abdominal exam
 - Tanner staging/Genital exam
 - Testotoxicosis: Increase in penis size, but testicular volume is less than expected for degree of sexual maturation
 - Androgen effects: clitoromegaly
 - Skin exam
 - McCune Albright: Large café au lait spots with irregular borders (Coast of Maine)
 - NF 1: Multiple café au lait spots with smooth borders
 - Androgen effects: Acne, hirsutism



Initial evaluation

- Bone age
 - All patients with advanced pubertal changes should have a bone age done
 - If normal, unlikely to have central precocious puberty
 - If advanced, requires further evaluation
 - Also would require further evaluation if normal bone age, but there is clinical evidence of central or independent precocious puberty



Further evaluation

- For boys, testosterone level can be useful
- Basal LH levels
 - Central: Pubertal
 - GnRH independent: Low
- GnRH stimulation
 - Central: LH and FSH levels increase
 - GnRH independent: LH and FSH levels do not increase



Further evaluation

- If based on previous studies, the child likely has central precocious puberty:
 - Brain imaging: MRI
 - Growth hormone levels—if previous CNS irradiation
- Idiopathic central precocious puberty is a diagnosis of exclusion



Further evaluation

- If based on previous studies, the child likely has GnRH independent precocious puberty, further work up is based on suspected diagnosis
- Can include:
 - Testosterone, estradiol, thyroid function tests, adrenal steroid precursors, hCG
 - Ultrasound: adrenal glands, uterus, ovaries, testes
 - Abdominal CT or MRI (Adrenal pathology)
 - Bone scan or skeletal survey (MAS)
 - Brain imaging: MRI



Treatment

- Central precocious puberty
 - Depends on etiology and pace of sexual maturation
 - If underlying cause, direct therapy at underlying cause
 - CNS tumor other than hamartoma: resection if possible
 - Radiation therapy is often indicated if surgical resection is incomplete
 - Removal of tumor rarely causes regression of precocious puberty
 - Otherwise, decision to treat is dependent on the rate of sexual maturation and the estimated adult height



Treatment

- Central precocious puberty
 - GnRH analogue



Treatment

- GnRH independent precocious puberty
 - Therapy is directed at underlying causes
 - Tumors of testes, adrenal gland and ovary: surgery
 - hCG secreting tumors: combination of surgery, radiation therapy, and chemotherapy depending upon site and histologic type
 - Defects in adrenal steroidogenesis: glucocorticoid therapy
 - Hypothyroidism: replacement therapy
 - McCune Albright Syndrome or Familial gonadotropin-independent precocity: treated with medicine that inhibit gonadal steroidogenesis
 - MAS: testolactone: inhibits aromatization of androgen to estrogen
 - FGIP: ketoconazole (inhibits androgen synthesis) or a combination of spironolactone (inhibits androgen action) and testolactone



Treatment

- Incomplete precocious puberty
 - No treatment is needed
 - Close follow up



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