Precocious puberty 1

(BMJ 2020;368:l6597, RCPCH 2013, Childhood and puberty close monitoring growth charts for boys and girls)

Red Whale
GEMS
Guidelines & Evidence Made Simple

Suspect precocious puberty if:

GIRLS <8y — **With onset of breast development and increased growth velocity** (0.2% affected)

BOYS <9y — **With genital development** Rarer (0.05% affected), but significant underlying cause more likely

History, examination and referral

All children with suspected precocious puberty should be referred. Urgent referral is sometimes required.

- **ALL boys require an urgent referral** because precocious puberty in boys is more likely to be due to a pathological cause.
- Certain features in the history/examination may help the paediatrician triage referrals (see table below).
- **In girls and boys, look for red flags in the history and examination (highlighted below). Examination may be normal but, in the presence of red flags in the history, urgent referral is still indicated.**

History (asynchronous order of stages of development/rapid changes make a pathological cause more likely):

- Which signs of puberty have been noticed? When? In what order did they appear? Rapid/slow progression?
- If vaginal bleeding has started, also consider other causes, e.g. non-accidental injury/abuse. Average age of menarche is 12.3y, usually around 2 years after the onset of breast development. If a girl presents with menarche <10y, consider asking about asynchronous puberty or earlier missed signs of precocious puberty.
- What age did the parents start puberty?

Examination should include neurological examination, genital examination and plotting growth on growth chart because this identifies those who need an urgent referral.

Initial investigations which *may* be carried out in primary care for boys and girls: LH, FSH, oestradiol and testosterone.

Referral urgency and red flags to look out for

History: red flag features	Examination	Urgency of referral
Girls and boys		
New onset of headaches, visual disturbance or signs of raised intracranial pressure (possible intracranial pathology).	Neurological examination, including fundoscopy and visual fields.	**Girls with any of these features should be referred urgently** (even if examination normal). **All boys should be referred urgently, even in the absence of any of these features. But if any of these features are present, highlight this in the referral letter to help the paediatricians decide exactly how urgent the urgent referral is!**
Polyuria/polydipsia (possible pituitary/hypothalamic cause).	Neurological examination, including fundoscopy and visual fields.	
History of a CNS disorder/injury, e.g. CNS trauma, meningitis, cranial irradiation, hypoxic-ischaemic injury, neurofibromatosis.	Neurological examination, including fundoscopy and visual fields.	
Steep increase in growth (may not be reported, may only be identified on plotting).	Plot height and weight: if growth crosses ≥1 centile space in 3–6m, this is a red flag.	
Pubic hair in infancy.	May signify pituitary or adrenal disorder or virilising tumour (testicular/ovarian).	
McCunne-Albright syndrome: genetic mosaicism. Hormonal secretion of autonomous ovarian cysts.	Unilateral café au lait macules, facial asymmetry or signs of hyperthyroidism/Cushing's syndrome.	
Boys only		
Genital enlargement (penile growth or testicular enlargement before 9y).	Examine for testicular mass/lump.	**All boys referred urgently but, if testicular lump, may follow different referral pathway.**
Girls only		
Clitoromegaly OR Menarche before 8y OR Progressive breast enlargement over 4–6m before 8y AND upward crossing of height centiles.	Genital examination for cliteromegaly. Plot height and weight on growth chart.	Urgent referral.
ALL other girls with precocious puberty.	Normal neurological and genital examination and normal growth.	Routine referral.

Precocious puberty 2

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Causes

1. Early commencement of GnRH secretion (= gonadotrophin-dependent precocious puberty (GDPP)):

- **Idiopathic:** commonest cause of GDPP, affects girls>boys (likely genetic and environmental components).
- **Central nervous system causes:** tumour/malformation of hypothalamus, germinomas, space-occupying lesions, congenital brain disorder, acquired brain injury/infection.
- **Genetic syndrome:** neurofibromatosis type 1, Sturge-Weber, tuberous sclerosis.

2. Increased sex steroid production independent of GnRH (= gonadotrophin-independent precocious puberty (GIPP)):

- **Virilising tumours:** androgen-producing (ovarian/adrenal), testicular Leydig cell or HCG-producing tumours.
- **Congenital adrenal hyperplasia.**
- **McCune-Albright syndrome**: hormone secretion of autonomous ovarian cysts.

Note: **Obesity in girls**: can give the *appearance* of breast development or can contribute to precocious puberty: increases oestrogen levels and aromatisation of androgens (accelerates development of sexual characteristics and growth).

Height and weight

- Height crossing ≥1 full centile space may indicate precocious puberty (e.g. from below 50th to above 75th centile).
- The RCPCH growth charts have 'puberty lines' that show the normal age limits for phases of puberty.
- Compare child's height centile with the mid-parental centile (details of this are on the growth charts above).
- A child whose height centile was similar to the mid-parental centile but then has rapid growth is more likely to have a pathological cause than if height has been consistently on a higher centile than mid-parental centile.

Features of puberty

- **Adrenarche:** activation of adrenal axis: causes increased secretion of androgens from adrenal glands.
- **Thelarche:** onset of breast development.
- **Pubarche:** development of pubic hair.
- **Menarche:** periods start.

Tanner staging (T)	Girls	Boys
Pre-puberty (T1)	No signs of pubertal development.	No signs of pubertal development.
In puberty (T2–3)	Any of the following: • Breast enlargement (with nipple enlargement). • Pubic/axillary hair.	Any of the following: • Slight deepening of voice. • Pubic/axillary hair. • Enlargement of penis/testes.
Completing puberty (T4–5)	All of the following present: • Started periods. • Breast development. • Pubic and axillary hair development.	Any of: • Voice fully broken. • Moustache/facial hair growth. • Adult-sized penis and pubic and axillary hair.

Management and counselling

Management in secondary care: if no serious cause, a watch and wait approach may be used to assess speed of changes.
Treatment of gonadotrophin-independent precocious puberty depends on the underlying cause (tumour, CAH, etc.).
For girls with idiopathic gonadotrophin-dependent precocious puberty (commonest cause):

- Some have no treatment (often if >6y of age).
- For some girls, GnRH analogues may be considered:
  - Helps preserve adult height potential if ≤6y; no evidence of benefit if older and puberty not progressing rapidly.
  - Sometimes considered to postpone menarche: secondary care/parents need to weigh up burden of injections against timing of menarche (untreated, menarche is often only a few months earlier than average).

Counselling:

- Height: children with precocious puberty who do not receive GnRH analogues reach a similar height to those treated.
- Periods: precocious puberty not treated with GnRH analogues: mean time to menarche after start of puberty is 4.5y.
- Breast cancer: increased lifetime risk following earlier menarche (epidemiological data).
- Other: possible association with metabolic syndrome/polycystic ovarian syndrome.