Delayed Puberty

Purpose of this guideline

- To aid evaluation of a child presenting with delayed or absent pubertal development
- To guide initial investigations and referral to paediatric endocrinology

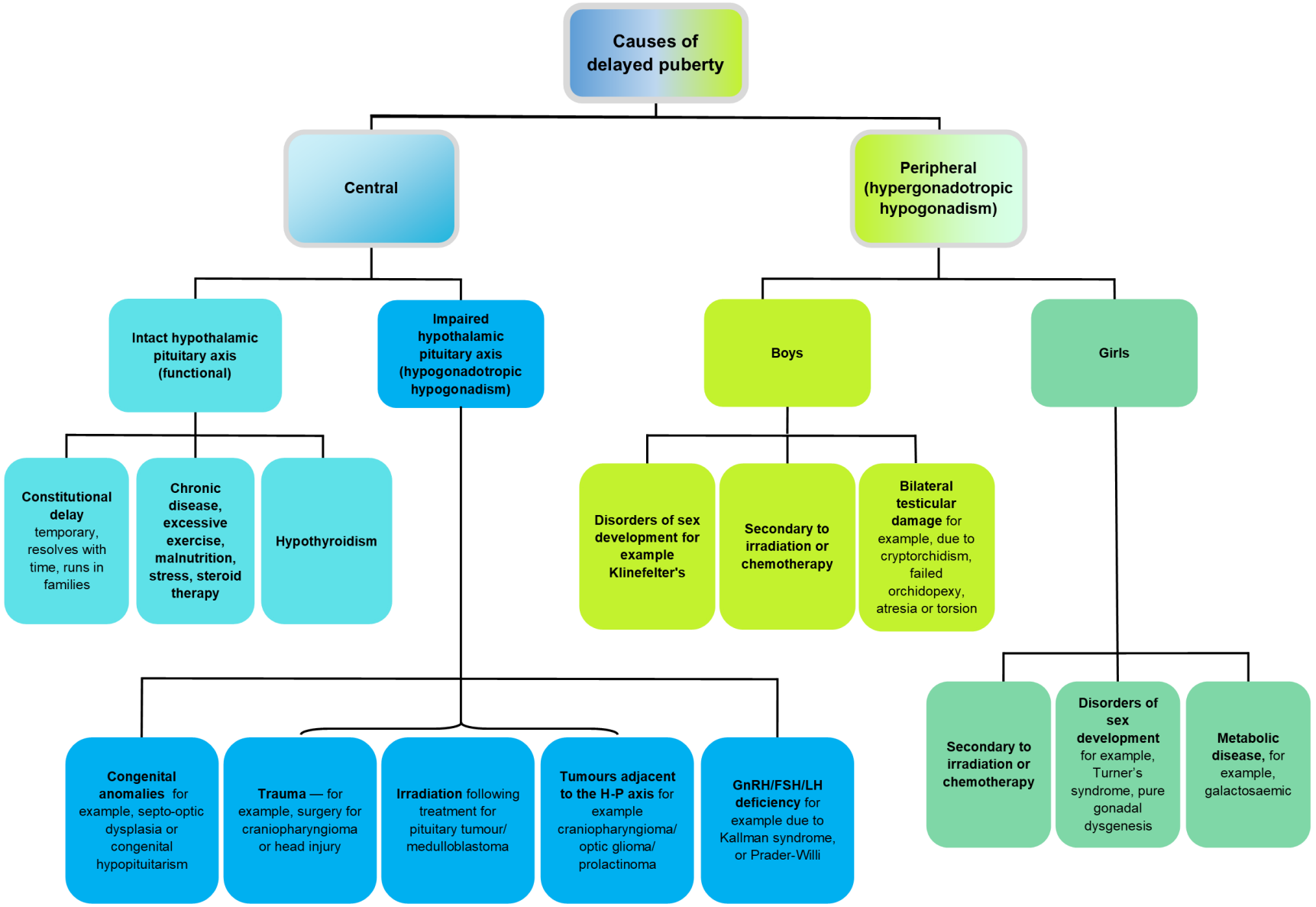
Definition

Puberty is delayed in girls if there are no pubertal changes by the age of 13.

In boys, puberty is delayed if there are no pubertal changes by the age of 14.

Delayed puberty is more common in males than females but occurs in about 2% of young people overall. Many young people initially present with concerns about their height rather than pubertal development itself.

Pubertal stage is more closely associated with bone age, i.e. skeletal maturity, than actual age.


Causes of delayed puberty
Central
Peripheral (hypergonadotropic hypogonadism)
Intact hypothalamic pituitary axis (functional)
Impaired hypothalamic pituitary axis (hypogonadotropic hypogonadism)
Boys
Girls
Constitutional delay temporary, resolves with time, runs in families
Chronic disease, excessive exercise, malnutrition, stress, steroid therapy
Hypothyroidism
Disorders of sex development for example Klinefelter's
Secondary to irradiation or chemotherapy
Bilateral testicular damage for example, due to cryptorchidism, failed orchidopexy, atresia or torsion
Congenital anomalies for example, septo-optic dysplasia or congenital hypopituitarism
Trauma — for example, surgery for craniopharyngioma or head injury
Irradiation following treatment for pituitary tumour/ medulloblastoma
Tumours adjacent to the H-P axis for example craniopharyngioma/ optic glioma/ prolactinoma
GnRH/FSH/LH deficiency for example due to Kallman syndrome, or Prader-Willi
Secondary to irradiation or chemotherapy
Disorders of sex development for example, Turner's syndrome, pure gonadal dysgenesis
Metabolic disease, for example, galactosaemic

Clinical features of puberty

In boys, the first sign of puberty is an increase in the size of the testes to ≥4mls. This is followed by an increase in penile size and pubic hair development. The growth spurt associated with male puberty is later than in females and usually starts about 1 year after puberty begins. This is because the testosterone levels need to be high enough for the excess to be converted to oestrogen to induce GH release.

In girls, the first sign of puberty is breast bud development, with pubic hair development beginning at around the same time. The growth spurt in girls occurs early in puberty. The average onset of menarche is 13 years, although there is geographical and ethnic variation.

Pubic hair can develop before the onset of puberty in boys and girls because of adrenal androgen generation which typically starts prior to pubertal onset.

What causes pubertal delay?

Constitutional delay of growth and puberty is common. It accounts for approximately 90% of cases, particularly in boys. It is likely to run in families, is transient, and puberty will start spontaneously. Delayed puberty can also be caused by external factors, such as chronic disease, excessive exercise, malnutrition and stress.

Other causes of delayed puberty can be grouped into central and peripheral causes:

Central delayed puberty (hypogonadotropic hypogonadism): Ovaries/testes are capable of producing sex hormone (oestrogen/testosterone), but there is insufficient stimulus from the pituitary or hypothalamus. Gonadotrophin levels (LH and FSH) and resultant sex hormone levels will be low.

Peripheral delayed puberty (hypergonadotropic hypogonadism): Hypothalamic-pituitary signalling is intact, but testes/ovarian function is impaired. Gonadotrophin levels will be elevated but resultant sex hormone levels will be low.

What are the important areas to cover in the initial assessment?

History of presenting complaint:

- Assess stage of puberty using Tanner staging criteria – see picture below
- Try and establish if young person has had a ‘growth spurt’
- Ask if any concerns regarding impaired sense of smell or mirror movements – could be suggestive of Kalman's syndrome (the association of gonadotropin deficiency with absent sense of smell)

- Recent change or excessive exercise patterns, any recent weight loss
- Recent excessive tiredness / constipation/ cold intolerance / weight gain– could be suggestive of disorders such as hypothyroidism
- Symptoms that could be suggestive of tumours adjacent to the H-P axis – visual problems, headaches, confusion or personality change, polydipsia / polyuria

Tanner stages of development.

Tanner stage	Male genital appearance	Male genital description	Female pubic hair appearance	Pubic hair description	Breast appearance	Breast description
1		Testicular volume <3ml		No pubic hair		Elevation of papilla only
2		Testicular volume <3ml, change in texture to scrotal skin		Sparse growth chiefly along the labia/base of penis		Breast bud stage
3		Increase in size of penis with further testicular enlargement		Darker, coarser, more curled hair		Enlargement of breast and areola
4		Further enlargment of penis and testicles with development of glans penis		Adult type hair over a smaller area		Projection of the areola and papilla
5		Adult size and shape		Spread to the medial surface of the thighs		Recession of the areola to the contour of the breast, projection of papilla only

Stephen H Bradley et al. BMJ 2020;368:bmj.l6597

Past Medical history:

- Any known chronic medical conditions or patterns of disordered eating
- Any previous surgery/radiotherapy to brain or abdomen/pelvis or chemotherapy
- Any previous torsion or undescended testes
- Previous mumps

Family history

- Pubertal timing of family members (average age of menarche is just prior to 13th birthday) and any known fertility issues

Social history:

- Impact of delayed puberty on young person – bullying is common and confidence can be affected

Examination:

- Pubertal staging – see Tanner staging above. Particularly assessment of breast bud development/ testicular size
- Systemic examination, checking for any dysmorphic features or signs of chronic disease
- Height and weight (including mid parental height and height velocity)

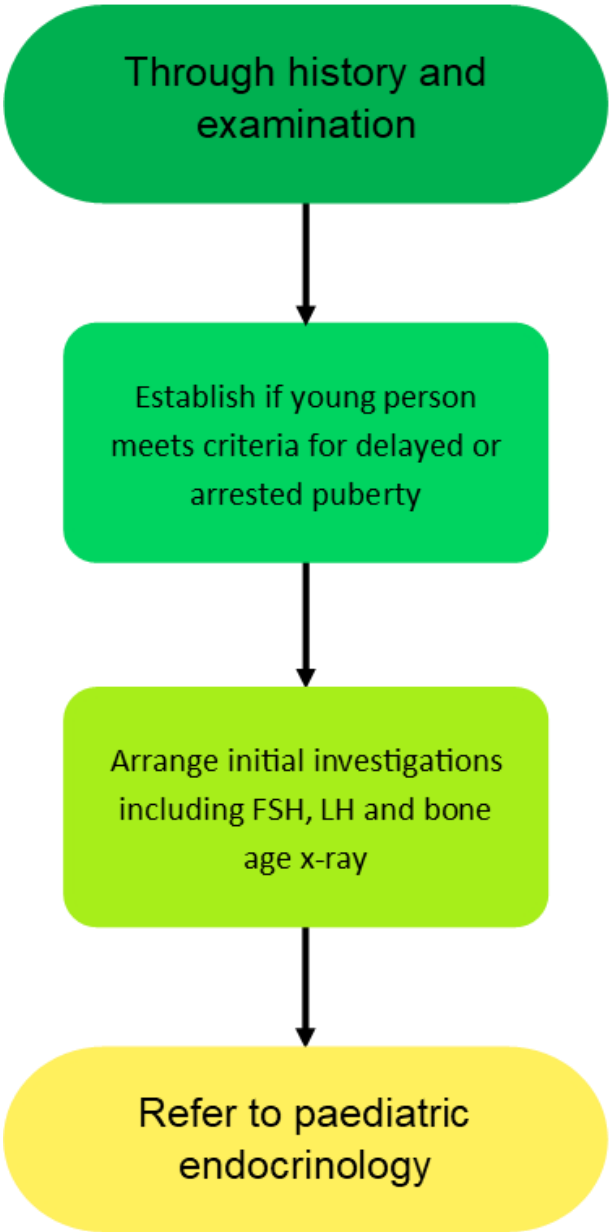
What initial investigations should be arranged?

- Chronic disease screen – FBC, U&Es, LFTs, TFTs, anti-TTG, ESR
- FSH, LH, prolactin, and oestradiol/testosterone
- Bone age x-ray

Who should be referred to paediatric endocrinology and how urgently?

Any patient who is confirmed to have delayed puberty should be referred to paediatric endocrinology.
Arrested puberty (any patient who has started puberty, but then stopped progressing) is a 'red flag' and may suggest serious underlying pathology so requires an urgent referral.
Once referred, the endocrinology team may consider additional investigations such as early-morning testosterone, karyotype, and a pelvic ultrasound. Depending on the symptoms and initial investigation results, an MRI head may also be appropriate.

Summary:



References

Guidelines produced using BMJ Best Practice and guidelines on delayed puberty produced and published by Kingston Hospital.
Tanner staging taken from BMJ, reference above.