



Child and adolescent growth disorders

An overview



BACKGROUND While many children presenting with apparent disorders of growth will be short or tall children growing normally, it is important to identify those children who have an underlying pathological cause. Parental expectation and anxiety will often accompany growth issues and this needs to be addressed.

OBJECTIVE The article aims to assist the clinician in distinguishing pathological short stature from normal variants, and to guide in the management of normal variants and common pathologies.

DISCUSSION Pathological short stature can be distinguished from normal variants by careful history and examination followed by accurate assessment of the growth parameters of height, weight, body proportions and growth velocity, and judicious use of investigations. Growth is a dynamic process that requires multiple measurements over time. If the patient has a nonpathological cause of short stature, explanation and reassurance are critical – for both the parents and child – to feel supported and comfortable with their height outcome.

Growth is one of the most fundamental tasks of childhood development. Adequate lengthening of the skeleton relies upon the complex interaction between genetic, hormonal, nutritional, and psychosocial variables. Attaining the maximum height potential for every child is a key component of the health professional's role in the care of young people. Parental expectation and anxiety will often accompany growth issues and this needs to be addressed when dealing with concerns around height potential.

Normal growth

The growth velocity in humans is greatest in late fetal life.¹ It then decreases until oestrogen mediated epiphyseal fusion occurs in adolescence, with the notable exception of the pubertal growth spurt. Growth rates are similar between the genders until puberty. The pubertal growth spurt is later and of higher velocity in males. This leads to a 50th centile height value of 177 cm for males and 164 cm for females.²

What is a growth disorder?

The most important distinction for clinicians to make is between a child who is short but growing well, and child who is growing poorly. Short stature is defined as a height below the 1st centile for age when plotted on the appropriate growth chart. However, one height measurement does not equal growth – growth is a dynamic process that requires multiple measurements of height. This should be done over a minimum of 6 months. A normal child's growth will be parallel to the centiles, but the child whose growth is falling off the centiles may have a pathologic cause of growth failure.

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Assessing growth

Assessment of a child's growth involves the measurement of:

- height plotted against standard centile charts
- weight plotted against standard centile charts
- body proportions, and
- growth velocity plotted against growth velocity centile charts.

Ideally, one person should measure the patient at every visit to exclude inter-observer bias. For height measurements, children less than 2 years of age should be placed on a supine table, with one measurer holding the child's head and the other performing the measurement. From 2 years of age, the child should be assessed using a stadiometer – the child should stand without shoes or socks, heels and back against the wall/board, head straight, and gentle upward pressure applied to the mastoid process.³ Normal body proportions are:

- arm span to total height ratio around 1.0 at all ages
- upper segment to lower segment ratio (upper segment is top of head to symphysis pubis) is around 1.7 as a neonate, decreasing to 1.4 at age 4–5 years, down to just below 1.0 by age 10–12 years.

To assess the growth velocity, serial measurements are required, preferably over 1 year. The growth in that time is then calculated (and converted to cm/year) (Figure 1). The growth velocity is a sensitive marker of the slowing of growth even when this is not apparent on standard centile charts,⁴ however plotting repeated height values on a standard chart usually gives a good indication as to the current growth velocity.

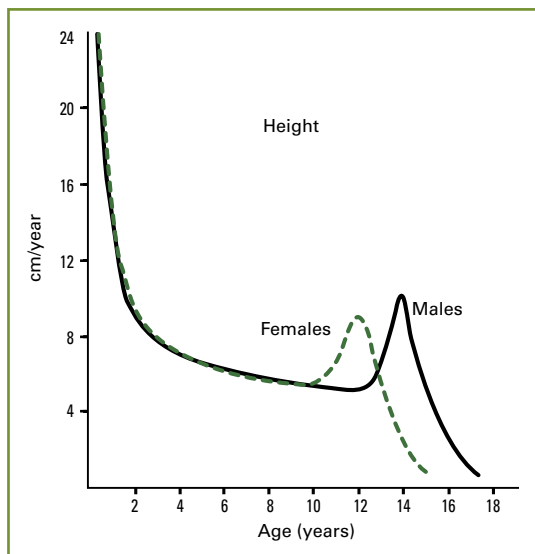


Figure 1. Growth velocity over childhood and adolescence (male and female)

Predicting adult height

To assess the child's likely height potential, the mother's and father's heights need to be ascertained, and then plotted. If the child is female, subtract 13 cm from the paternal height and then plot it on the female chart to get the correct centile. The mother's height is then also plotted on the chart, and the midpoint between these values is the mid parental height (MPH). Conversely, if the child is male, add 13 cm to the mother's height and plot on the male centile chart, then plot the father's height on the same chart and again take the midpoint to find the MPH. The 3rd and 97th centile for the child are 10 cm to either side of the MPH.⁵

To ascertain a more precise height prediction for a child, a bone age (X-ray of wrist and hand) needs to be performed. Based on the bone age, chronological age and current height, the clinician or radiologist can determine the likely height outcome for that child using the Bayley-Pinneau tables.⁶

Interpreting growth data – normal variants

The most important task in the assessment of short stature is to determine if it is a normal variant of growth, or due to an underlying pathological condition. The two normal variants that may present with short stature are:

- familial short stature, and
- constitutional/maturational delay in development.

In constitutional delay there is a transient slowing of growth at approximately 3 years and again at 11–12 years of age; there may be a family history of delayed growth and pubertal development. Bone age, height age (the age at which height would be at the 50th centile) and

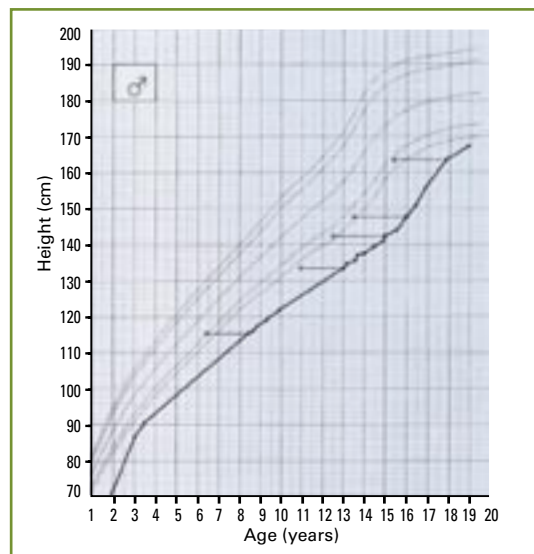


Figure 2. Growth chart of a boy with constitutional delay with correction for bone age

growth velocity can assist in distinguishing constitutional delay from familial short stature (Table 1). Figure 2 shows a typical growth chart with corrections for bone age of a child with constitutional delay. Patients with familial short stature are all likely to be short adults, but children with constitutional delay in development are likely to end up with a good height outcome as their delayed bone age reflects physiologically delayed growth.

Pathological causes of short stature

Indicators of possible pathological causes of short stature on history and examination are summarised in Table 2 and 3. It is especially important to ascertain birth weight and look for symptoms and signs of chronic illness, psychosocial issues and other features on examination such as dysmorphism.

The most important discriminator between pathological short stature and the normal variants described above is the height velocity – a child who has slowed growth and is ‘crossing the centiles’ is far more likely to have a pathological aetiology and investigation and/or appropriate referral is required. The weight can also be a vital clue toward interpreting short stature, with loss of weight (ie. the weight falling off the centiles) commonly preceding slowed growth, therefore raising the possibility of chronic illness, nutritional or psychosocial causes. Features indicating a likely pathological cause and appropriate investigations are outlined in Table 4 and 5.

Importantly, all female patients presenting with short stature (height <1st centile) and who do not clearly meet the criteria for a normal variant (see above) should have a karyotype performed to exclude Turner syndrome.

Table 1. Comparing constitutional growth delay with familial short stature

	Constitutional delay	Familial short stature
Height	Short	Short
Bone age	Delayed	Not delayed
Growth rate	Slow	Normal
Height age	Same as bone age	Less than bone age
Height prognosis	Good	Poor

Table 2. Features to consider on history in assessment of short stature

- Birth weight/length
- Family heights and maturational history
- Systems review for chronic illness including respiratory, renal, gastrointestinal, cardiac and general development
- Psychosocial history

(Females with complete or partial absence of one X chromosome may have features of Turner syndrome, which include short stature, broad chest, widely spaced nipples, webbed neck, and other system disorders such as cardiac defects, renal anomalies and hypothyroidism).

Pathological conditions causing short stature can be committed to memory using the mnemonic ‘Endocrine PICNICS’: (not in order of incidence) (Table 6).

Treatment of short stature

The treatment for short stature is largely dependent upon the underlying aetiology. If the patient has a nonpathological cause of short stature, explanation and reassurance are critical for both the parents and child to feel supported. Irrespective of the diagnosis, exploring issues around school, sport, and family are important to help encourage these patients to feel comfortable with their height outcome. Using examples of short people who have achieved in all walks of life and encouraging the child to ‘think tall’ will greatly assist in the improvement of self esteem for this potentially vulnerable group. In particular, the involvement of specialised social work support for individuals and groups with short stature may be as important as medical intervention.¹⁰

Boys with constitutional delay of puberty may benefit from induction of puberty by testosterone administration.^{11,12} This will lead to commencement of

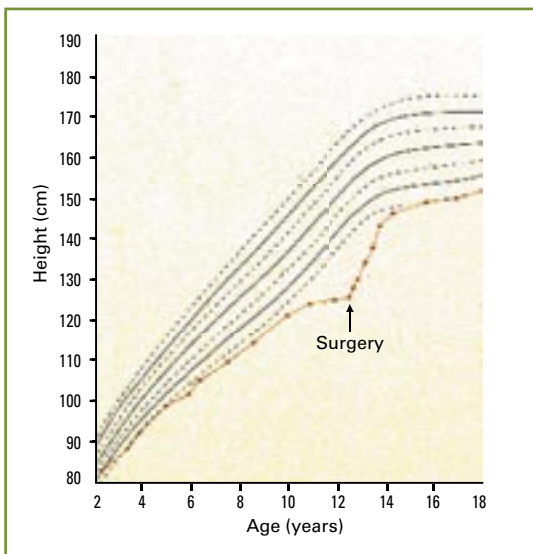


Figure 3. Growth chart of a girl with Crohn disease (note improvement of growth postpartial colectomy)

normal pubertal development including the pubertal growth spurt, with minimal impact on height potential, and will help the adolescent to fit in with his/her peer group. This treatment should only be undertaken by a specialist centre, and would not be considered until the patient was at least 13.5–14 years of age. Females with extreme constitutional delay can be treated with low dose oestrogen, however this may cause premature epiphyseal fusion and must be undertaken with caution.

Catch up growth is seen in many of the conditions listed once other parameters are controlled (eg. if exogenous steroids can be ceased).¹³ The catch up growth may not reach the patient's premorbid height potential, but should be to within two standard deviations of the MPH, assuming the cause for short stature has been treated. This is clearly not applicable to conditions where therapeutic interventions are not 'curative', such as in Turner syndrome.

If a pathologic cause is suspected, referral to a paediatric endocrinologist may be appropriate. If it is felt the patient meets the criteria for growth hormone therapy (*Table 7*), then an application may be made to the central governing body.

Tall stature

Tall stature is a far less common presenting problem than short stature, as it is often less of a concern to parents. The vast majority of these patients will have familial tall stature. As with short stature, serial measurements to determine the duration of the problem, and plotting the father's and mother's heights to look at basic genetic inherited potential need to be the initial steps in assessment. Again, it is important to note if the child is 'crossing the centiles', as this is far more likely to have an underlying pathological basis. Investigation should then include thyroid function testing, IGF-1, karyotype, and bone age.

Familial tall stature

The patient will have a tall parent, and may have a family history of early puberty. A bone age can be helpful in demonstrating the advancement in development and aid in predicting final height.

Endocrine causes

- Hyperthyroidism: usually a recent increase in growth velocity and other typical symptoms such as anxiety, heat intolerance and palpitations
- Precocious puberty: all children who have accelerated growth should be assessed for signs of pubertal

development. In girls <8 years of age and boys <9 years of age, pubertal development may represent precocious puberty from a number of underlying aetiologies and specialist opinion should be sought. While these children may be tall at diagnosis, they will end up with a reduced final height due to premature fusion of their epiphyses due to the prematurely high circulating levels of oestrogens and androgens¹⁴

- Growth hormone secreting tumours: these are extremely rare in paediatrics.

Syndromal causes

There are numerous uncommon syndromes with tall stature as a feature – the majority are rare. The more

<p>Table 3. Features to consider on examination in assessment of short stature</p> <ul style="list-style-type: none"> • Specific systems • Body proportions (arm span/segmental ratios) • Dentition/other midline defects • Visual fields/fundi • Thyroid exam
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<p>Table 4. Features suggesting pathological cause and requiring further investigation</p> <ul style="list-style-type: none"> • Child <1st centile • Abnormally short for family heights • History/exam suggests chronic illness (especially weight loss more than height loss) • Abnormal growth velocity (<25th centile) • Body proportions abnormal • Dysmorphic features or midline defects <p>If no investigations undertaken, measure 3–6 monthly for 12 months, then annually to ensure normal height velocity</p>
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<p>Table 5. Investigations to consider in assessment of short stature</p> <ul style="list-style-type: none"> • full blood examination, erythrocyte sedimentation rate, electrolytes, coeliac screen • Calcium and phosphate • Thyroid function • Bone age • Karyotype (females) • Provocative growth hormone testing, eg. glucagon stimulation testing or the insulin tolerance test

Table 6. Causes of pathological growth: Endocrine PICNICS

		Mechanism	Features
Endocrine	Hypothyroidism	Thyroid hormone promotes long bone growth	Weight gain, lethargy, poor school performance, constipation, dry skin, neonatal jaundice, bradycardia
	Growth hormone (GH) deficiency		Cleft lip and palate or midface hypoplasia, neonatal hypoglycaemia, increased fat to lean body mass ratio
Psychosocial iatrogenic	Cushings syndrome	Excess glucocorticoid slows linear growth	Weight gain, cushingoid features
	Deprivation	Decreased GH secretion ⁷	
	Glucocorticoid use Spinal irradiation	Shortened vertebral bodies	Cushingoid features Lower upper segment: lower segment ratio
Chronic illness	Gastrointestinal, eg. inflammatory bowel disease (<i>Figure 3</i>) or coeliac disease	Poor nutrition	Loss of weight or failure to gain weight
	Renal, eg. chronic kidney failure or renal tubular acidosis Haematological disorders Complex congenital cardiac disease Cystic fibrosis Metabolic disorders		Features of the underlying disorder
Nutritional		Inadequate nutrition	Loss of weight in absence of other findings Siblings may also be affected
Intrauterine growth retardation	Unknown aetiology or part of a syndrome, eg. Russel-Silver syndrome ⁸		Hemihypertrophy, triangular face for Russell-Silver syndrome
Chromosomal	Turner syndrome Down syndrome Prader-Willi syndrome		Features of the syndrome
Skeletal dysplasia	Eg. achondroplasia (autosomal dominant)		Disproportionate short stature Skeletal deformity FH of skeletal dysplasias ⁹

common syndromes are:

- Klinefelter syndrome: 47XXY males have a phenotype that includes tall stature, eunuchoid body habitus, poor musculature, sparse body/ facial hair, small testes,¹⁵ and an aggressive impulsive personality. Klinefelter syndrome is a frequently missed diagnosis, often not being picked up until the patient and his partner present with primary infertility
- Marfan syndrome: an autosomal dominant condition caused by a defect in the fibrillin gene leading to hyperextensibility, arachnoidactyly, kyphoscoliosis, aortic root problems, lens dislocation, and high arched palate. Patients with multiple endocrine neoplasia type IIB have a similar phenotype
- Sotos syndrome: also known as cerebral gigantism,

Table 7. Indications for growth hormone therapy in Australia

- Essential criteria – patient <1st centile with growth velocity over 1 year <25th centile
- Growth hormone deficiency on provocative testing
- Turner syndrome

characterised by rapid growth in early childhood with acromegalic features, likely due to an as yet unrecognised hypothalamic defect

- Homocystinuria: an autosomal recessive disorder with a similar phenotype to Marfan syndrome with additional

problems of poor bone density and an increased tendency to thrombosis

- Beckwith-Wiedemann syndrome: a fetal overgrowth syndrome with features including macrosomia, hepatosplenomegaly, macroglossia and hypoglycaemia, and a risk of malignancy, especially Wilm's tumour.

Treatment of tall stature

The majority of patients with tall stature will require only simple reassurance, with advice on predicted height based on family history of timing of puberty and bone age. If significant concerns remain, sex steroid administration will reduce the final height by causing premature fusion of the epiphyses. In particular, the use of oestrogen on constitutionally tall girls has been considered standard practice in the appropriate clinical setting for many years.¹⁷ However, changing social perceptions of tall stature, coupled with recent studies which have shown impaired fertility in women treated with oestrogen for tall stature,¹⁸ have led to this treatment now only being used in rare cases, and after much deliberation and specialty input.

Conclusion

There are a multitude of diagnostic possibilities for children with growth disorders. However, with a careful history and examination followed by accurate assessment of growth parameters and judicious use of investigations, patients with a true growth disorder can be identified. If no pathologic process is suspected, it is vital to provide reassurance to patients and their families along with a clear explanation of the reasons why this conclusion has been reached. Ongoing follow up of patients with concerns about growth is of crucial importance to both further alleviate anxiety and to confirm that the patient is following the growth course predicted by the initial diagnosis. The importance of effective support provided by both medical staff and other groups such as social work and community and support groups cannot be underestimated. Referral is often required to manage patients with an underlying disorder due to the complexity and relative infrequency of many of the conditions discussed above.

Conflict of interest: none declared.

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