As tall stature becomes more prevalent and more acceptable, referrals, particularly of tall girls, appear to be decreasing. The referral of a child with tall stature is frequently the result of parental concern about actual or future final height. However, knowledge of the pathogenesis, clinical and biochemical associations and potential treatment of tall stature is clinically relevant.

**Pathogenesis and differential diagnosis**

Tall stature is usually associated with one of three aetiological categories. In order of frequency these are: familial advanced growth; a syndrome associated with tall stature, which has usually been present since infancy; and an abnormal increase in growth rate of endocrine origin. The differential diagnosis is shown in Table 4.1.

**Assessment of the child or adolescent with tall stature**

Repeated height measurements are essential for the assessment of tall stature. The combination of auxology, careful history-taking and physical examination will exclude the need for laboratory investigations in most cases. Procedures needed for the clinical assessment of a child or adolescent referred with tall stature are given in Table 4.2.

**Investigations**

Patients with intellectual delay may well have had previous investigations. If physical examination is completely normal and the child comes from a tall family, investigations are usually not indicated. Regular height measurements will be sufficient. If abnormalities are detected in the history or on examination, basal investigations are indicated, as shown in Table 4.3.

Further investigations will be dictated by the results of the baseline tests. If the diagnosis of excess growth hormone (GH) secretion caused by a GH secreting pituitary adenoma is considered, investigation should proceed as shown in Table 4.4.

**Protocol for glucose tolerance test**

Give 1.75 g carbohydrate orally (up to maximum of 75 g = two glasses of Lucozade). Serum GH at: -30, 0, 30, 60, 90, 120 and 150 minutes. Normal GH suppression is a value of <4 mU/L at some time during the test.

**Causes of tall stature**

**Familial tall stature or constitutional advanced growth**

This is the most common cause of referral of patients for tall stature. If the patient is a girl, it is frequently the mother who, having suffered herself from being tall as a child and adolescent, is concerned about her daughter. In groups of tall children, GH secretion has been shown to be statistically elevated when compared to normal or short stature children. However, in an individual child excess GH secretion is not usually apparent.

The tall stature is usually noticeable by primary school entry. Physical examination is normal. Assessment of bone age, which is likely to be advanced, and calculation
Chapter 4

The likelihood of earlier than average puberty should be explained. Reassurance and growth monitoring are the principles of management.

Syndromes associated with tall stature
These disorders will not be described in detail. They are all rare; however, the principal phenotypic features of three important tall stature syndromes—Sotos’, Marfan’s and Beckwith–Wiedemann syndrome—are given in Table 4.5.

Endocrine causes of tall stature
The three endocrine causes of tall stature should be suspected after clinical examination. All will require hormone investigations to confirm the abnormality. Specialist referral at this stage is recommended.

GH secreting pituitary tumour
A GH-secreting tumour causes tall stature and gigantism in childhood and adolescence, and acromegaly in adult life. An association with McCune–Albright syndrome is recognized. Because of its extreme rarity in childhood, this disorder should be managed jointly with an adult endocrinologist, who will have far more experience. Suppression of GH secretion may require pituitary surgery, radiotherapy, somatostatin analogue or GH receptor antagonist therapy.

Treatment of familial (constitutional) tall stature
Occasionally, the degree of anxiety surrounding advanced growth, usually in girls, is so great that treatment is indicated to try to slow down growth and therefore reduce final height. Two forms of therapy are currently used:

Table 4.1 Differential diagnosis of tall stature.

| 1 | Familial tall stature |
| 2 | Syndromes associated with tall stature: |
|   | chromosomal defects |
|   | Klinefelter’s syndrome |
|   | XXXY, XYY syndromes |
|   | overgrowth syndromes |
|   | Sotos’ syndrome |
|   | Weaver’s syndrome |
|   | Marshall–Smith syndrome |
|   | Beckwith–Wiedemann syndrome, hyperinsulinism |
|   | Marfan’s syndrome |
|   | MEN 2B |
|   | ACTH resistance |
|   | Homocysteinuria |
| 3 | Tall stature of endocrine origin: |
|   | GH secreting pituitary tumour |
|   | precocious puberty |
|   | hyperthyroidism |
| 4 | Simple obesity |

Abbreviations: ACTH, adrenocorticotrophic hormone; GH, growth hormone; MEN, multiple endocrine neoplasia.

Table 4.2 Procedures for the assessment of a patient with tall stature.

- Height, weight, height velocity
- Heights of parents, siblings
- Birth weight, length, head circumference
- History of previous growth, past medical history
- Intellectual development
- Systematic inquiry
- Examination for dysmorphic features
- Systematic examination
- Pubertal development staging with measurement of testicular volume
- Bone age and final height prediction

Table 4.3 Baseline investigations for tall stature.

- Karyotype
- T4, TSH
- IGF-I
- Bone age and final height prediction

Abbreviations: IGF-I, insulin-like growth factor; T4, thyroxine; TSH, thyroid-stimulating hormone.

Table 4.4 Investigations for suspected GH secreting pituitary adenoma.

- Glucose tolerance test for GH secretion
- MRI scan of pituitary
- Visual fields
- Cortisol (9.00 a.m.)
- Prolactin
- Testosterone, LH, FSH (depending on age)

Abbreviations: FSH, follicle-stimulating hormone; LH, luteinizing hormone; MRI, magnetic resonance imaging.
Tall stature

When to involve a specialist centre

- Dysmorphic syndromes associated with tall stature.
- Tall stature associated with excess GH secretion.
- Difficult cases of tall stature associated with hyperthyroidism or precocious puberty.
- GH receptor antagonist treatment is likely to become established as the treatment of choice for constitutional tall stature.

Controversial points

- The treatment of tall stature in girls is controversial.

Table 4.5 Principal clinical features of Sotos’, Marfan’s and Beckwith–Wiedemann syndromes.

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Clinical Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sotos’ syndrome</td>
<td>Increased birth length, recognizable facies, hypotonia, clumsiness, early puberty</td>
</tr>
<tr>
<td>Marfan’s syndrome</td>
<td>Autosomal dominant, fibrillin gene defect, arm span 8 cm &gt; height, kyphoscoliosis</td>
</tr>
<tr>
<td>Beckwith–Wiedemann syndrome</td>
<td>Increased birth weight and length, growth velocity and bone age advanced, macroglossia</td>
</tr>
</tbody>
</table>
High-dose oestrogen therapy is rarely practised now. Treatment with a somatostatin analogue may be effective but is invasive and associated with side-effects. New therapy using a GH receptor antagonist is promising but not yet established to be beneficial.

- As tall stature is better tolerated by society, there seems to be less indication for therapy.
- Rare conditions, such as GH secreting pituitary tumours, are very infrequently seen in paediatric practice. These patients must be managed jointly with an adult endocrine unit.

**Potential pitfalls**

- Failure to consider the diagnosis of or examine the patient carefully enough for dysmorphic features suggestive of Marfan’s syndrome. This diagnosis may have serious consequences as these patients need life-long cardiovascular surveillance.
- Failure to appreciate that tall stature and delayed puberty are an unusual combination. An important differential diagnosis is Klinefelter syndrome, which should be considered.

**CASE HISTORY**

A 9-year-old girl was referred because of tall stature. She was in good health. On examination there were no dysmorphic features. Her height was just above the 97th centile and her parents’ heights were on the 90th and 97th centiles. Pubertal development was: breast, stage 2; axillary hair, stage 2; pubic hair, stage 3; and no menarche.

Baseline investigations (Table 4.3) were all normal. Consequently, an endocrine cause of her advanced growth was not identified. Bone age was 12.4 years and final height prediction was 188 cm. The parents, particularly the mother who had suffered as a result of her own tall stature, enquired about treatment. The child was not particularly concerned. Treatment was not advised.

**Question**

Are any further investigations indicated?

**Answer**

Probably not. She had occasional headaches so a magnetic resonance imaging (MRI) scan of the pituitary was performed which showed a pituitary gland with a convex upper border but no suprasellar extension. She also had a height velocity of 9.2 cm/year. She therefore had an oral glucose tolerance test for GH suppression. Her GH levels during the glucose tolerance test suppressed to 0.5 mU/L, indicating that there was no evidence of increased GH secretion.

Diagnosis: constitutional (familial) advanced growth.

**References and further reading**


