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# Growth Retardation: An Approach to Management


## SUMMARY

The physician who looks after children and teenagers is often confronted with the problem of short stature or growth failure. A major concern is when, and how extensively, to investigate the problem. From a practical standpoint, assessment can be related to height percentiles. The aims of treatment are to identify and treat appropriately the patients in whom there is an organic cause and to provide psychologic counselling and support. Common causes of growth failure are identified and a simple approach to management is outlined. (Can Fam Physician 1985; 31:1039-1043)

## SOMMAIRE

Le médecin qui soigne des enfants et des adolescents est souvent confronté avec le problème de petite taille et de retard de croissance. Une des préoccupations importantes est de savoir quand et jusqu'où investiguer le problème. D'un point de vue pratique, on peut établir une relation entre l'évaluation et l'échelle de taille en percentiles. Les buts du traitement sont d'identifier et de traiter adéquatement les patients présentant une cause organique et de fournir un counselling et un support psychologique. L'article mentionne les causes les plus fréquentes du retard de croissance et propose une approche simple au management de ces cas.


**Key words:** Growth retardation, children, management

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GROWTH IS A complex phenomenon which involves genetic, environmental, nutritional, hormonal and psychological factors.

Growth retardation can be a major cause of concern and anxiety to children, adolescents, parents and physicians. It is defined as height more than two standard deviations below the mean (the fifth percentile being approximately two standard deviations from the mean), or marked decrease in growth velocity.[1]

Linear growth and weight gain or loss are extremely sensitive indicators of a child's basic health. The physician will identify problems causing impaired growth more easily by obtaining growth measurements and recording them on percentile charts.[2] Common causes of growth failure are conditions characterized by intrinsic shortness such as familial short stature, chromosomal and dysmorphic syndromes, severe intrauterine growth retardation, and certain bone dysplasias such as the chondrodystrophies; constitutional delay in growth and puberty; and conditions characterized by nutritional, endocrinological, or chronic disease problems. Primary endocrine disease, such as growth hormone and thyroid hormone deficiency, probably accounts for less than 10% of growth retardation in children. It is important, however, not to overlook problems in endocrine dysfunction; the people in Fig. 1 demonstrate the natural history of untreated hypopituitarism. A deficiency in factors important to growth may retard growth (see Table 1).

## Types Of Growth Retardation

Growth rate varies with age and sex. Between birth and six months, infants

should grow at least 16 cm. From six to 12 months, length should increase at least eight centimeters in both sexes. Between one and two years, girls grow at least 11 cm and boys at least ten centimeters. Both boys and girls should grow six centimeters per year between age two and five years. After age five, up to the beginning of rapid adolescent growth, growth below 4.5 cm per year is subnormal in both sexes.

Determination of the level of epiphyseal maturation or 'bone age' is often helpful in evaluating children with abnormal growth. Greulich and Pyle's standards[3] are the most widely used. A delayed bone age is commonly associated with constitutional delay in growth and puberty, nutritional disorders, endocrinopathies such as growth hormone deficiency and thyroid hormone deficiency, and severe chronic disease.

Usually the linear growth curve of a child from age three years until puberty follows a track that closely approximates a specific percentile. Crossing percentiles (e.g., dropping from the 50th percentile for weight and height to the 25th percentile, or accelerating from the 25th percentile to the 50th percentile) during the first three years of life is not uncommon, and reflects genetic, intrauterine, nutritional and childhood infectious influences. Deviations from percentile growth after three years should be carefully evaluated.

Linear growth disorders can be categorized as intrinsic shortness, delayed growth, and acquired growth failure (attenuated growth).[4] The differential diagnosis of these basic growth disorders is given in Table 2.

Children with intrinsic shortness have inherent limitations to bone growth, that destine them to be short adults. Growth curves in these children are below, but approximately parallel to, normal percentiles.[4] The growth rate is usually within normal limits but may be subnormal; the bone age approximates the chronological age.

Children with a delayed growth pattern (e.g., constitutional growth delay) have late puberty, continue to grow for longer than most of their peers, and ultimately reach a normal adult height. The characteristic growth curve is below but parallel to the normal growth channel. Fall-off in growth usually occurs over the first three years of life;[5] after age three or four yearly growth increments are normal. The bone age is delayed and represents an excellent prognostic sign for future linear growth.

Children with attenuated growth have a clearly subnormal growth rate.[4] The bone age is usually delayed. Children with attenuated growth patterns virtually always have endocrine, metabolic, or systemic disease. It is essential that these children be diagnosed and appropriately treated.

## Managing Growth Retardation In Children

The age at which growth retardation was first evident may provide a diagnostic clue (see Fig. 2). The birth history is important. If the birth weight and length are small for gestational age, search for intrauterine causes of growth retardation. Many small-for-dates infants grow slowly after birth. Those babies who attain the fifth percentile by age one are likely to reach a low normal adult height. On the other hand, a significant proportion of the

**TABLE 1**
**Factors Influencing Growth**

| |
|---|
| **Genes** |
| Familial short stature |
| Constitutional growth delay |
| Turner's syndrome |
| Trisomies |
| **Nutrients** |
| Deficient intake (e.g., anatomical defect) |
| Defect in digestion (e.g., disaccharidase deficiency) |
| Defect in absorption (e.g., celiac disease) |
| Defect in transportation of storage (e.g., glycogen storage disease) |
| **Cartilage and Bone** |
| Chondrodystrophy |
| **Oxygen** |
| Congenital heart disease |
| Chronic respiratory disease |
| Chronic infection or inflammation |
| Chronic renal disease |
| Chronic chest infection |
| **Environment** |
| Pregnancy (e.g., small for dates baby) |
| Birth (e.g., hypoxia) |
| Emotional deprivation |
| Drugs (e.g., ritalin, amphetamine, cortisone) |
| **Hormones** |
| Hypothyroidism |
| Growth hormone deficiency |
| Hypogonadism |

**Fig. 1. The short subjects (aged 20-32 years) have untreated anterior pituitary insufficiency, including growth hormone deficiency. The two tallest subjects (aged 24 and 26) are their siblings. (Reproduced, with permission, from McKusick VA, Rimoin DL. General Tom Thumb and other midgets. Sci Am 1967; 217:102-11.)**

small-for-dates babies may not reach the fifth percentile; their growth continues parallel to but below the fifth percentile and, as adults, their height will be below the lowest limits of the normal range. Traumatic labor and delivery and perinatal hypoxia may be associated with subsequent growth impairment.

Fall-off in linear growth during the first three years may reflect either a congenital or intrinsic problem, constitutional delay in growth which is a normal variant, or an acquired problem such as hypothyroidism, undernutrition, or chronic systemic disease. Growth retardation detected later in life may reflect any one of these basic disorders.[4] A thorough systems review should reveal most acquired systemic diseases. Notable exceptions are hypothyroidism, occult renal disease and asymptomatic gastrointestinal disease (e.g., celiac syndrome and inflammatory bowel disease). These illnesses may present with the only overt sign being growth retardation. It is equally important to obtain the history of the patient's past health.

Previous heights and weights, if available, should be plotted on the growth chart. Height below the fifth percentile and diminished growth rate can then be easily discerned. Be aware that the potential for short or tall stature varies among ethnic and racial groups (e.g., North American Indians and Inuit tend to be shorter than Canadian whites). Standard growth charts are not always valid in identifying abnormal growth for such patients. The family history provides additional information about genetic illness, racial origin, and developmental and social patterns of the family. In particular, attempt to record the heights and onset of puberty in siblings, parents and grandparents. Such information may suggest a familial pattern of short stature or constitutional delay in growth and puberty.

Perform a careful and complete physical examination; this will usually identify the common causes of growth impairment. The height and weight, the arm span, pubis-to-heel length and head circumference should be measured. Identification of abnormalities of body proportion may help confirm a diagnosis. For example, in normal children and those with proportional short stature, the arm span is approximately equal to the height. One of the features of achondroplasia is shortness of the extremities, which can be confirmed by finding an arm span less than the height. In general, the head circumference of children with proportional short stature should be at or above the fifth percentile; a head circumference of less than the fifth percentile suggests a central nervous system lesion. The stage of sexual development should be recorded in all children with short stature.

The major concerns in assessing growth retardation are when, and how extensively, to investigate the problem. Evaluate children whose height is below the fifth percentile or whose linear growth is deviating from the percentile along which it had been progressing. In the latter instance, in the child over age three, yearly linear growth increments will be less than 4.5 cm per year.

## Height At Or Just Below The Fifth Percentile

Often parents will bring children to a physician, complaining that they are short. The past history and systems review are unremarkable and previous growth records are unavailable. The child's height plotted on the growth chart is at or just below the fifth percentile.

In such a situation it is sufficient to obtain only a bone age radiograph and offer supportive counselling, provided that the physical findings are normal and there is a history of familial short stature or growth delay. The bone age radiograph is helpful in predicting future growth and ultimate height. The child's height should be measured and charted annually to ensure that growth is parallelling the fifth percentile.

Alternatively, the physician may be dealing with a similar but slightly different situation in which the history and physical findings are apparently normal, but the child is at or just below the fifth percentile and there is no history of short stature or delayed development in the family tree. In this situation, obtain a serum thyroxine value to exclude hypothyroidism and, in girls,

**TABLE 2**
**Classification of Growth Retardation[4]**

| | Intrinsic Shortness | Delayed Growth | Attenuated Growth |
|---|---|---|---|
| **Differential Diagnosis** | Familial (normal variant)*<br>Genetic syndromes<br>—chromosome anomalies<br>—bone dysplasias<br>—dysmorphic syndromes<br>Severe intrauterine growth retardation<br>—intrauterine infections<br>—placental insuffiency (e.g., from smoking) | Constitutional delay in growth and puberty (normal variant)*<br>Moderate chronic disease (e.g., anemia or repeated infections)<br>Undernutrition | Endocrinopathies<br>—GH deficiency<br>—hypothyroidism<br>—Cushing's syndrome<br>—Sex hormone deficiency (after age 12)<br>Acid/base disturbance<br>Severe chronic disease (e.g., Crohn's disease)<br>Severe malnutrition<br>Spinal irradiation |
| **Yearly Linear Growth Increment** | Normal or subnormal | Usually normal after age three years, but may be subnormal | Subnormal |
| **Bone Age** | Approximates chronological age | Delayed | Delayed |

* most common

do chromosome studies to exclude Turner's syndrome (gonadal dysgenesis). Our clinic group believes that chromosome studies are warranted in girls if the height is more than 2.5 standard deviations below the mean; if the height is below the fifth percentile and decreasing and there is no other obvious cause for the growth failure; or if physical stigmata suggests gonadal dysgenesis. Again, a bone age radiograph is of prognostic value. The child and family should be counselled and followed annually. Further investigations are indicated if linear growth deviates from the fifth percentile.

If previous growth records are available, an accurate growth chart can be constructed. When growth has consistently been at the fifth percentile, there is usually a family history of short stature or delayed growth. If the physical findings are entirely normal, then determining the bone age and subsequent counselling will be sufficient. The patient should be measured and counselled annually.

## Height Deviating From A Previous Percentile

In this situation, growth records will be available and it will be obvious the patient's height is deviating from the percentile along which it had been progressing. The problem must be investigated. In many instances, the diagnosis will be apparent and the initial investigations will be indicated by the findings on history and physical examination. If there are no clues to the problem from the history and physical findings, consider the following tests:

- CBC and erythrocyte sedimentation rate;
- urinalysis;
- serum thyroxine, calcium, phosphorus and alkaline phosphatase values;
- blood urea nitrogen values;
- carbon dioxide tension;
- bone age, skull and chest radiographs;
- stool examination for ova and parasites; and
- chromosome analysis (in girls below the fifth percentile).

If these investigations do not indicate a cause for the growth failure, investigate pituitary function; in particular, assess the adequacy of growth hormone release. The diagnosis of growth hormone deficiency is clear-cut when there is a subnormal growth hormone response (less than seven micrograms per liter) to more than one type of stimulation test. In Canada, the most commonly used pharmacological screening test for growth hormone deficiency is the levodopa/propranolol test. Other pharmacological tests to measure growth hormone reserve are the insulin tolerance test and the arginine stimulation test. Physiological tests of growth hormone release involve blood sampling following exercise and sleep. Normal children seldom have a random growth hormone level high enough to indicate normal reserve.

## Height Three Standard Deviations Or More Below The Mean

The patient whose height is three standard deviations or more below the mean for his or her age should first be investigated fully, as described in the last section. It is advisable to have a consultant who is experienced in problems of short stature to share in the investigation and management.

## Constitutional Growth Delay

When a child or teenager presents complaining of short stature, the most likely cause statistically will be constitutional delay in growth, a condition characterized by diminished growth rate which is particularly evident during the first three years;[5] delayed bone age (detected by radiography of the wrist and comparing epiphyseal and bone maturation to the standard set by Greulich and Pyle[3]); normal laboratory

**Fig. 2. Characteristic growth retardation patterns plotted against a growth curve.**

*** May also reflect acquired disease (e.g., chronic systemic disease) and certain endocrinopathies (e.g., growth hormone or thyroid hormone deficiency).**

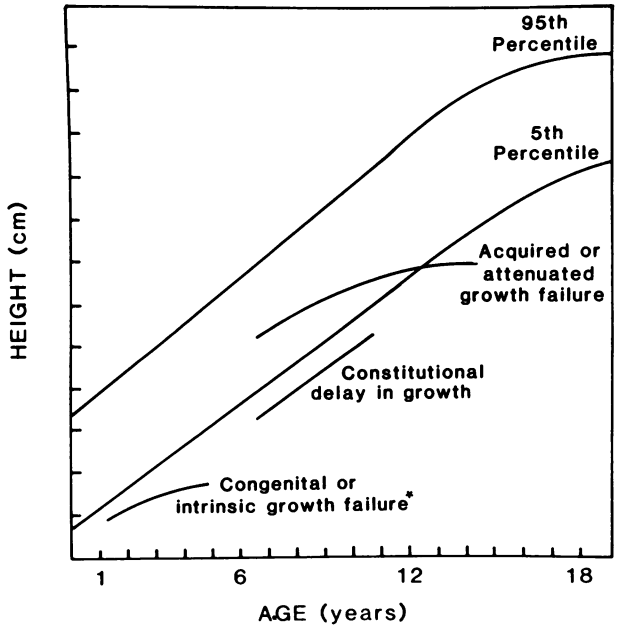
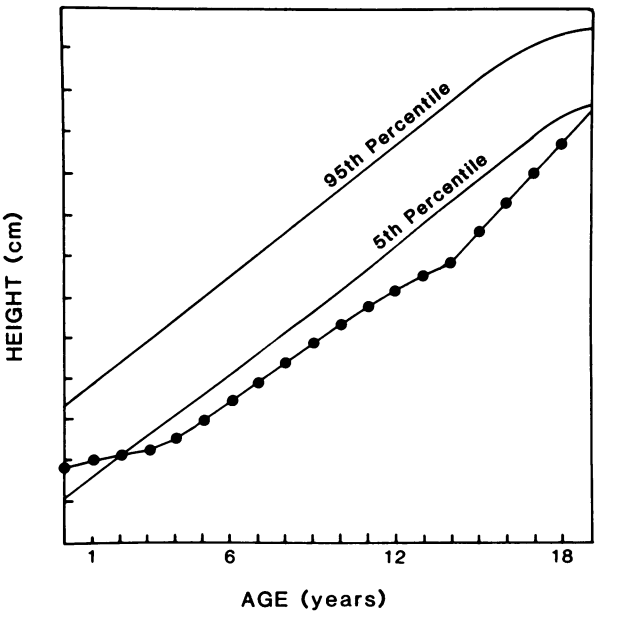



**Fig. 3. Characteristic growth pattern of a child with constitutional delay in growth and puberty.**



findings, including values of thyroxine and growth hormone; and absence of chronic systemic disease.

Puberty is often delayed by one to several years. The classical growth pattern of a person with constitutional delay in growth is illustrated in Fig. 3. The decline in growth occurs during the first several years of life. These children are often misdiagnosed as failing to thrive in the early years. There is usually a family history of 'late bloomers' (delayed puberty and late termination of linear growth). The prognosis is excellent; these children ultimately reach a normal adult height. It will, however, take them longer than their peers and linear growth often continues until age of 21 or later.

Constitutional growth delay is distinct from familial short stature. The child is well in all respects, except that he or she is short; puberty is usually not delayed, and there is a family history of short stature. The child's bone age approximates the chronological age. Because bone age is normal, linear growth potential is not as great as in the child with constitutional growth delay.

## Treatment

In general, there are two goals in managing short stature: identifying and appropriately treating patients in whom there is an underlying organic cause, and psychologic counselling and support.

The child and parents should be given a frank and thorough explanation of the reasons for the growth problem. Realistic predictions of future growth rates and ultimate adult height can be based on the underlying problem, degree of skeletal maturation, previous growth records and family heights.[6]

Patients with constitutionally delayed growth ultimately reach a normal adult height, but do so later than their peers. The benefits of androgen treatment in boys with constitutionally delayed growth have now been established.[7] Testosterone enanthate at 200 mg per month for three to four months, given after age 14 will induce pubic hair growth and accelerate growth without undue skeletal maturation. Such treatment does not stimulate 'extra growth' but does permit the boy to reach his potential height more quickly.

The use of growth hormone in treating so-called 'normal short children' is controversial.

## Biosynthetic Human Growth Hormone

Van Vliet et al.[8] have demonstrated that some short, but otherwise normal, children with normal blood levels of growth hormone may benefit from intramuscular injections of pituitary growth hormone three times weekly. Such findings may be encouraging for some short children, particularly in view of the advent of human growth hormone manufactured through genetic engineering. The authors, however, emphasized that until we have more knowledge of the long-term effect of growth hormone and possible adverse actions, and more sharply defined criteria for selecting patients and dosage regimens, indiscriminate treatment of short, normal children with the hormone is unwarranted.

Underwood et al.[9] reported on uses and possible abuses of biosynthetic human growth hormone. They raise many questions about the potential use of growth hormone in treating normal short children.[9] Such questions include:

- How does one identify the patients who will respond to therapy without subjecting all such children to a growth hormone trial lasting six to 12 months?
- Will prolonged treatment produce a taller adult?
- What are the possible side effects to growth hormone treatment?

Possible side effects may include the development of hypothyroidism (observed in growth hormone deficient children who had been treated with growth hormone); the formation of antibodies to growth hormone; glucose intolerance; hyperlipidemia and the possibility of acceleration of atherosclerotic processes; bony overgrowth; and complications from hypercalciuria. Animal studies suggest that some tumors are growth hormone dependent, but there is no evidence to implicate the hormone in human carcinogenesis.

The need for education about growth hormone is reflected by athletes' recent interest in growth hormone, as a way to increase their strength and athletic performance.

Underwood[9] believes that there is an urgent need for therapeutic trials to determine the effect of growth hormone in short children who do not have a growth hormone deficiency. In Canada, such trials should be approved by appropriate scientific and ethics committees. ◉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