Etiologies and Early Diagnosis of Short Stature and Growth Failure in Children and Adolescents

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Accurate measurement of height and weight using standardized techniques is a fundamental component of pediatric medical visits. Calculation of height velocity over time enables comparison with standardized growth charts to identify potential deviations from normal. Growth deviations may be expressed as SD from the normal population mean for children of comparable age and sex; children with heights >2 SD below the mean are generally classified as short stature. In a child with suspected impaired growth, a detailed evaluation should be conducted to identify the cause. Such an evaluation may include a combination of personal, family, and social history; physical examination; general and perhaps specialized laboratory evaluations; radiologic examinations; genetic testing; and consultation with a pediatric subspecialist, such as a pediatric endocrinologist. Variants of normal growth include familial short stature, constitutional delay of growth and puberty, and small for gestational age with catch-up growth. Pathological causes of abnormal growth include many systemic diseases and their treatments, growth hormone deficiency, and a series of genetic syndromes, including Noonan syndrome and Turner syndrome. Children with short stature in whom no specific cause is identified may be diagnosed with idiopathic short stature. Early identification of abnormal growth patterns and prompt referral to specialist care offer children with growth failure and/or short stature the greatest chance for appropriate diagnosis, treatment, and improved clinical outcomes. *(J Pediatr 2014;164:S1-S14)*.

Auxology is the science of growth and development. For the practicing pediatrician, auxology is applied in the evaluation and measurement of growth through widely validated clinical methods, used daily for the evaluation of normal child maturation and identification of deviations from normal. Measuring length or height, weight, and head circumference in infants and younger children is a fundamental component of pediatric medical visits, allowing for the early identification of growth alterations or abnormalities potentially associated with concomitant treatable conditions or known genetic syndromes.[1] Proper measurement techniques must be used consistently. Subsequent plotting of measurements on appropriate growth charts with careful monitoring and interpretation of changes over time may ensure prompt specialist referral for children with growth abnormalities.[1-4] Such childhood growth abnormalities may manifest as slow or excessive gains in height, weight, or both. In this report, we focus on the diagnostic evaluation of children with short stature owing to any of a variety of causes.

How to Measure Growth

Key evaluations used to determine growth in children over time include measurements of length or height, weight, and head circumference.[1,3] Determination of the circumference of the waist, hips, and neck and measurement of skin folds may provide additional information on growth in selected children.

Length is usually the measurement of choice in children aged <2 years, and height is the standard measurement for children aged >3 years.[3] Between 2 and 3 years of age, both measurements often are recorded to allow comparison with previous length measurements and to provide new reference values for assessment of later increases in height. The importance of proper technique when measuring length and/or height cannot be overstated. Ideally, infants are measured for length in a firm box with an inflexible board and fixed headboard, and children are measured for height while standing erect against a wall-mounted stadiometer. Tips to help ensure accurate length and height measurements are provided in **Figure 1**. Both length and height should be recorded to

BMI	Body mass index	MGRS	Multicenter Growth Reference Study
CDC	Centers for Disease Control and Prevention	MPH	Midparental height
		NS	Noonan syndrome
CDGP	Constitutional delay of growth and puberty	PE	Physical examination
		PWS	Prader-Willi syndrome
GH	Growth hormone	SGA	Small for gestational age
GHD	Growth hormone deficiency	SHOX	Short stature homeobox
HV	Height velocity	TH	Target height
IGF-1	Insulin-like growth factor 1	TS	Turner syndrome
ISS	Idiopathic short stature	WHO	World Health Organization
IUGR	Intrauterine growth restriction		

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Supported by Novo Nordisk.

Please see the Author Disclosures at the end of this article.

0022-3476/$ - see front matter.

http://dx.doi.org/10.1016/j.jpeds.2014.02.027

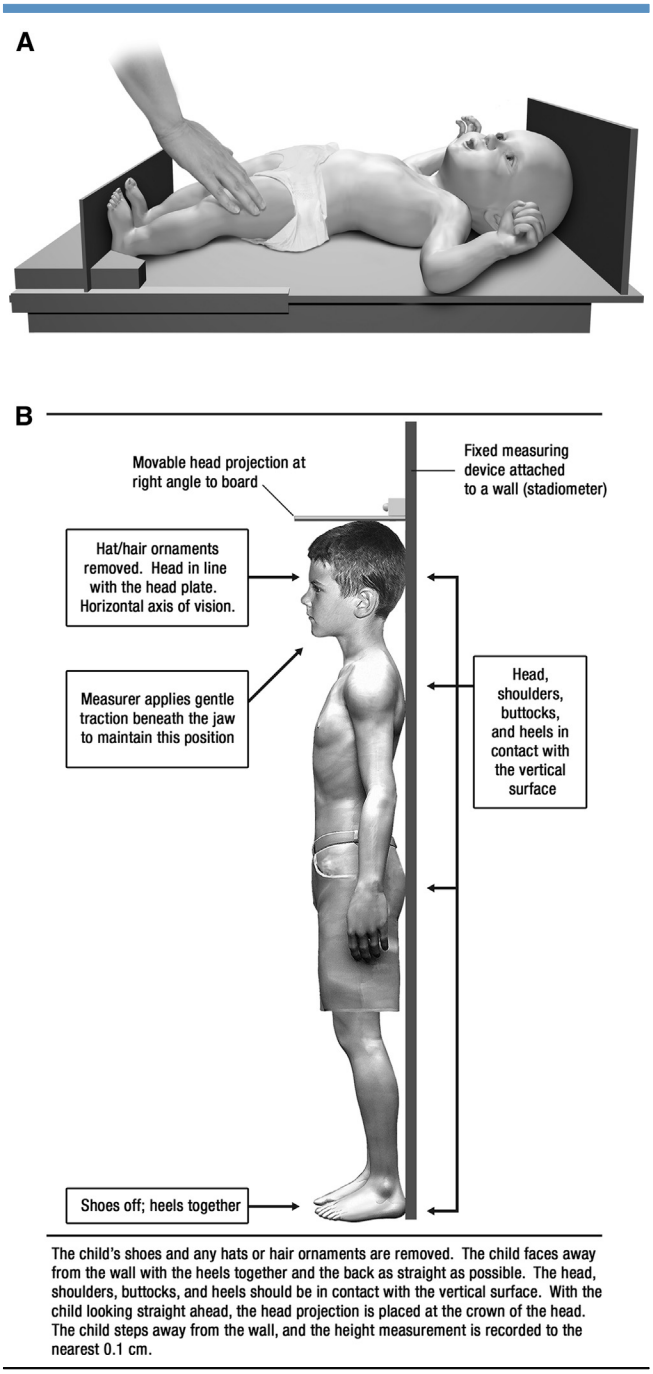

Figure 1. **A,** Infant length measurement technique. (Content and design by SPOON Foundation. Reproduced with permission from the Joint Council. Copyright © 2013, Joint Council. All rights reserved.) **B,** Height measurement technique.[10] (Adapted with permission from: Rogol AD. Diagnostic approach to short stature. In: Basow DS, editor. UpToDate. Waltham, MA: UpToDate; 2013. Copyright © 2013 UpToDate, Inc. For more information, visit www.uptodate.com.)

the nearest 0.1 cm[5] and measured twice, with results of the 2 measurements falling within a 4-mm range.[6] If the difference between the 2 values is >4 mm, then a third measurement should be obtained, with the average of the 2 closest values recorded. In a busy primary care office, a single carefully obtained measurement is usually considered sufficient if the value is consistent with the child's growth curve.

Accurate weight measurement depends on the accuracy and correct calibration of the scale. It is critical that the child be weighed without shoes and wearing only light clothing.

Techniques to evaluate growth have been standardized, including the routine use of growth charts as recommended by the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC).[7-9] The 2006 WHO international growth standard charts represent growth standards for healthy children in optimal conditions and are now recommended as the preferred instruments for plotting growth in children aged <24 months. The CDC charts, used in the past for infants as well as children and currently recommended for children and adolescents aged 2-20 years, are reference charts documenting growth over time, as observed in subjects included in the data collection process.

The differences between these 2 chart types reflect their origins. Data used to create the WHO charts were obtained from the Multicenter Growth Reference Study (MGRS) conducted between 1997 and 2003 in 6 cities located in 6 different countries (Brazil, Ghana, India, Norway, Oman, and the US [California]). The MGRS was based on the hypothesis, later proven, that young children have similar growth potential independent of ethnicity and place of birth. When raised in a healthy environment and adequately nourished, children aged <24 months included in the MGRS reached comparable mean lengths in all 6 countries. Of note, children were excluded from the MGRS according to a number of criteria, including low socioeconomic status, breastfeeding for <12 months, maternal smoking during pregnancy or lactation, perinatal morbidities, and child health conditions known to affect growth. The CDC growth charts are based on data collected over time from 5 cross-sectional, nationally representative health examination surveys. For the growth charts for children aged <36 months, data were derived from the National Health and Nutrition Examination Surveys I, II, and III, conducted in the US from 1971 to 1994. From these surveys, the only exclusions were infants with very low birth weight. For the growth charts for children aged 2-20 years, data were derived from the National Health and Nutrition Examination Surveys I, II, and III as well as from the earlier National Health Examination Surveys II and III, conducted from 1963 to 1970.

Calculation of height velocity (HV) facilitates identification of a child's growth trajectory over time and evaluation of potential deviations from normal. While recognizing the potential for notable variation in HV among healthy children, the "rule of fives" can be used to estimate normal growth rates at various ages during childhood (**Figure 2**).[10] This convention suggests that growth may be rapid, at a rate of ~25 cm/year from birth to age 1 year, then moderate, at an average of 10 cm/year, from age 1 to 4 years.[10] In particular, children typically grow ~12 cm from age 1 to 2 years and 8 cm from age 2 to 3 years.[11] The rule of fives then suggests that growth further slows to ~5-