A Name behind a Syndrome

The Diagnostic and Prognostic Importance of Neonatal Length Measurements

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Growth is a masterful orchestration of a complex process that starts with conception and ends at the termination of puberty. During that period — which extends under normal circumstances until age 15–16 years in girls and 17–19 years in boys — there are periods of faster and slower growth velocity, depending on a variety of growth-stimulating factors and substrate availability [1–4]. There are four major periods of growth: intrauterine (9 months), infancy (2 years), prepubertal (6 or 7 years), and puberty (5–6 years in girls and 6–8 years in boys) [5,6].

The most impressive growth velocity takes place *in utero,* where during a period of 9 months the fetus grows from the microscopic sizes of an ovum, sperm and blastula to a 48–52 cm human being at birth [7]. In Israel, irrespective of ethnic origin, the mean length at birth is 50–50.7 cm in boys, and 49.7–50.5 cm in girls [8]. It is evident that the normal newborn achieves 26–29% of his or her adult height during the 9 months of gestation. The postnatal growth-stimulating hormones are growth hormone/insulin-like growth factor 1, and thyroid and sex hormones, the latter active only during puberty [9]; however, the factors that affect intrauterine growth are only partly known. One of the major factors, also documented by experimental studies [10], is fetal nutrition [11]. The endocrine control seems of limited influence [12], since the thyroid hormone-deficient fetus is of normal size, and growth hormone, IGF-I and insulin deficiency cause only a 10–15% reduction in the newborn's length [13–17].

In recent years, intrauterine growth estimates are performed using ultrasonographic methods [18]. Exact measurements, however, require expertise. Neonatal length is easy to measure [19,20], and is done by stretching the baby and using an infant anthropometer (Pedo Baby-JMB Ets-Belgium, or Rollametre-Castlemead Ltd., UK). Only the Pedo Baby can be used inside incubators [20]. The measurements can also be done with simpler instruments. Body growth is measured by length and height, and the estimation of nutritional status by weight for height or skinfold thickness.

The accurate measurement of neonatal length is of great importance and should be performed in every baby. The length should be plotted on infant growth charts according to gestational length [21]. Despite the fact that the range of variation of birth length is relatively small, it is necessary to establish whether the growth is adequate for age, and to observe the early postnatal growth velocity. Short stature at birth may be caused by a variety of genetic diseases affecting either the growth-stimulating hormones [12–17] or target organ non-responsiveness, such as in easily diagnosed bone or metabolic diseases (i.e., dyschondroplasias, mucopolysaccharidosis, etc), or chromosomal abnormalities. Since many of these babies — even those with deficient growth hormone or IGF-I (Laron syndrome) — may have normal body weights, weight alone is a misleading index for growth.

Also, the inverse is true. Some babies are born thin and of low weight or underweight, but their length is normal. This is true if there is a defect in the intrauterine nutrition in the third trimester of pregnancy.

Newborns who are short and of low weight may be either prematures — who are prone to catch up to normal size within the first 2 years of life [22,23] — or belong to the large group of so-called intrauterine growth retardation, a group that only rarely shows a catch-up growth (Laron, unpublished). The etiology of this type of growth retardation is multifactorial [24,25]. In addition to an early hormone imbalance, some of these factors seem to be linked to a placental insufficiency in the first weeks of pregnancy due to a vascular disturbance caused by malformations of the uterus, maternal smoking, or maternal vascular diseases including diabetes. Each of these factors affects the placenta. There may well be other so far unidentified causes. In recent years it has been found that prenatal factors influencing intrauterine growth affect health in adults [26,27]. Some of these infants may develop various metabolic abnormalities, including glucose

IGF-1 = insulin-like growth factor

intolerance, that are manifested even early in life [28,29] and predispose many of them to develop hypertension, heart disease, insulin resistance and diabetes in adult life [30].

The differential diagnosis and the decision to conduct more than routine laboratory investigations in a newborn with subnormal length depends on the gestational and family history, physical examination and blood chemistry. Growth hormone deficiency is easily diagnosed by a simple blood determination [31]. Genetic abnormalities in the growth hormone axis [32] should be considered in a short, well-nourished baby with hypoglycemia, with or without a micropenis. Insulin insufficiency is characterized by hyperglycemia. Serum IGF-I is of no value since the normal values are low; IGF-binding protein-3 is indicated if primary low IGF-I secretion, unrelated to growth hormone resistance, is suspected. X-ray of the femur head helps to estimate the skeletal (biological) age. This is usually done only if thyroid dysfunction (normal sized baby) is suspected. In case of phenotypic abnormalities, chromosomal (karyotype) and genetic analyses may help to diagnose a series of syndromes associated with short stature [33].

In conclusion, accurate measurement of body length at birth is extremely helpful in the diagnosis of abnormal growth, in the growth follow-up, in the prognosis of final height, and in the consideration of possible therapeutic intervention.

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