OPINION

The use of local reference growth charts for clinical use or a universal standard: A balanced appraisal

S. Milani[1], J.M.H. Buckler[2], C.J.H. Kelnar[3], L. Benso[4], G. Gilli[5], I. Nicoletti[6], G. Faglia[7], G. Radetti[8], G. Bona[9], Y. Schonbeck[10], S. Van Buuren[10], M. Hermanussen[11], G. Grugni[12], N. Marazzi[12], P.B. Júlíusson[13], M. Roelants[14,15], K. Hoppenbrouwers[15], R. Hauspie[14], R. Bjerknes[13], H. Lejarraga[16], and A. Sartorio[12]

[1]Section of Medical Statistics and Biometry, University of Milan, Milan, Italy; [2]Honorary Senior Lecturer, Department of Paediatrics, University of Leeds, Leeds; [3]Section of Child Life and Health, University of Edinburgh, Edinburgh, UK; [4]Professor of Auxology, University School of Motor Sciences; [5]Department of Neonatology, University of Turin, Turin; [6]Centro Studi Auxologici, Florence; [7]Professor Emeritus of Endocrinology, University of Milan, Milan; [8]Department of Paediatrics, Regional Hospital, Bolzano; [9]Division of Pediatrics, Department of Medical Science, University of Piemonte Orientale, Novara, Italy; [10]Netherlands Organization for Applied Science (TNO), Department of Child Health and Department of Statistics, Leiden, The Netherlands; [11]Aschauhof, Altenhof, Germany; [12]Istituto Auxologico Italiano, IRCCS, Division of Auxology and Experimental Laboratory for Auxo-endocrinological Research, Milan and Verbania, Italy; [13]Section for Pediatrics, Department of Clinical Medicine, University of Bergen, Bergen, Norway; [14]Laboratory for Anthropogenetics, Vrije Universiteit Brussel (VUB), Brussels; [15]Department of Youth Health Care, Katholieke Universiteit Leuven, Leuven, Belgium; [16]Consultant of Hopital Garrahan, Buenos Aires, Argentina

A much-debated topic is whether a growth chart should be local, national or international. On the one hand, if we consider that, by definition, a reference chart describes the anthropometry of a given population, we can conclude that we need as many reference charts as the number of different populations, no matter whether their anthropometric differences are ascribable to ethnic characteristics or to environmental, nutritional, socioeconomic, and health conditions. On the other hand, if we believe that all healthy children under unrestricted conditions fully express their growth potential, and that growth potential varies between individuals but not between populations, then a unique standard should apply to all children.

TARGET POPULATION: REFERENCE AND STANDARD

The terms "growth reference" and "growth standard" are still erroneously used as synonyms, leading to confusion on this topic. In auxology, a "reference" differs from a "standard" on the basis of the criteria used to define the target population, i.e. the population on which the chart is built and to which the chart will apply.

Target population

A target population is defined by a set of inclusion criteria (typically, geographical area, ethnic group, sex) and exclusion criteria, i.e. the presence of those factors known or supposed to affect growth, such as genetic disorders, congenital anomalies, severe infectious and metabolic diseases, prolonged nutritional restriction.

Reference

In the absence of exclusion criteria regarding risk factors for growth, a chart based on such a population is a reference, which describes ''how growth actually is'' in that population (1). Centers for Disease Control and Prevention growth charts for the US (2) are a reference in the sense that they are explicitly descriptive, although the authors recognize that some compromises were made on developing a true reference (3). The growth charts based on children affected by congenital diseases such as Turner's syndrome (4), cystic fibrosis (5), neurofibromatosis (6) should be regarded as references for these particular pathological conditions.

A reference chart reflects the genetic characteristics of healthy children belonging to a given population, as well as the prevalence of risk factors for growth in that population. Therefore, the differences between reference charts of different populations may be due to both genetic and non-genetic factors, whereas the differences between reference charts pertaining to different social groups or different periods of the same population denotes differences in health conditions. Actually, as asserted by Tanner (7), growth is a mirror of the condition of society.

The clinical use of a reference raises two methodological problems. The first one is that the centiles of the growth reference, which is essentially a descriptive tool, are used as decision limits. The other is that a reference might possess low sensitivity in detecting a child with growth anomalies, since the reference includes also children who may have been exposed to risk factors for growth. The first problem is intrinsic to the concept of

Key-words: Children, growth, reference growth charts.

Correspondence: A. Sartorio, MD, Istituto Auxologico Italiano, IRCCS, Laboratorio Sperimentale Ricerche Auxo-endocrinologiche, Via Ariosto 13 - 20145 Milan, Italy.

E-mail: sartorio@auxologico.it

Accepted January 3, 2012.

reference values defined on a statistical basis, in the field of laboratory medicine, some four decades ago (8). As to the second problem, from a practical viewpoint, when we deal with a population with low prevalence of risk factors (such as the populations of developed countries), the clinical use of a reference can be safely accepted.

Standard

To avoid the methodological weakness of the clinical use of a reference chart, we may adopt highly restrictive criteria which, excluding all children exposed to any known risk factor for growth, converge to define the characteristics of subjects enjoying good health and without nutritional or environmental constraints. Altogether, these characteristics constitute an "ideal" and somewhat unrealistic model to which a child or adolescent should conform, and the basis for a "prescriptive standard" or "norm" that indicates "how growth ought to be" (1). Unfortunately, such a model critically depends on which factors are taken into account, e.g. the socioeconomic conditions.

Do we really need, however, as many standards as the number of different populations? If the main reason for the differences that are observed between different reference charts is the inequality in health between poor and rich populations, these differences are expected to vanish when the restrictive exclusion criteria that define a standard population are adopted. In this case, the same unique standard could apply to all populations. On the contrary, if ethnic groups maintain their anthropometric differences even when selective inclusion and exclusion criteria are adopted, the very idea of unique standard for all must be rejected.

THE WORLD HEALTH ORGANIZATION CHILD GROWTH STANDARDS

The World Health Organization (WHO) child growth standards (9) are based on the assumption that a unique standard fits all, since the standard depicts "normal human growth under optimal environmental conditions and can be used to assess children everywhere, regardless of ethnicity, socio-economic status and type of feeding" (10). Nevertheless, even full-term single-born healthy children of non-smoking women from a favorable socio-economic background still show a residual difference in size at birth that is correlated with ethnicity – for example, a 1.4 cm difference in birth length between Norwegian and Indian neonates (11). A unique standard may be the right or the wrong choice depending on whether such differences are regarded as negligible or not (12).

The extent to which the anthropometric differences between ethnic groups are the result of genetic factors rather than health, nutritional, socioeconomic, and environmental conditions is still debated (13). Anyhow, the differences in neonatal size between countries involved in the WHO's study are likely ascribable to genetic differences, since the residual potentially harmful external conditions are expected to affect somatic growth in the fetal period even less than in the post-natal period, because of the protected uterine environment. As a matter of fact, undernutrition in pregnancy was found to stimulate a compensatory placental growth, capable of preventing fetal growth restriction (14).

A recent study (15) comparing Belgian and Norwegian infants and young children with the WHO standard showed persistence of population differences in growth even when using the same strict inclusion criteria as WHO. This suggests genetic or unknown environmental factors responsible for the differences.

THE ITALIAN SOCIETY FOR PAEDIATRIC ENDOCRINOLOGY AND DIABETOLOGY (ISPED) GROWTH REFERENCES

As regards late childhood, adolescence, and adulthood, conspicuous differences in somatic growth can be observed, also within the same country. As an example, data in the Italian Society for Paediatric Endocrinology and Diabetology (ISPED) series, covering all ages from 2 to 20 yr (16, 17), show different growth patterns between central-northern and southern regions of Italy. These differences had been reported in the past by many authors (18), but were never documented systematically, mainly as regards body mass index (BMI). At the end of the 20th century, children were still taller in central-northern than in southern Italy during the whole growth period: at the end of growth the average differences was 2.4 (girls) and 2.7 cm (boys). After puberty, BMI values of children in southern Italy became higher than those of children in central-northern Italy. At 18 yr of age, the prevalence of overweight (BMI>25 kg/m^2) and obesity (BMI>30 kg/m^2) in southern Italy was 27.4% and 4.5% (boys), and 19.3% and 3.5% (girls), respectively. These percentages were much higher than in central-northern Italy, where the prevalence of overweight and obesity was 16.7% and 1.8% (boys), and 10.0% and 1.3% (girls), respectively. Differences in height were unlikely due to environmental conditions, socioeconomic factors, nutritional intake, and lifestyle, all these being suitable for allowing each girl or boy to reach their target, at least in the last two decades. This is supported by the fact that the secular increase in adult height of Italian conscripts slowed down and nearly halted at the end of the 20th century: about 1.2 mm in central-northern Italy and 2.5 mm in southern Italy between 1995 and 1999 (19). We know that large genetic differences between central-northern and southern Italy exist, for instance in the incidence of some genetic disease, such as thalassemia, or in the distribution of blood groups. By contrast, wide differences in diet and physical activity could have been the reason why the prevalence of overweight and obesity was, and still is, much higher in southern Italy.

CONCLUSION

A reliable growth chart, i.e. a chart useful from a clinical perspective, should detect subjects at risk of disease and premature death, independently of ethnic origin. As an example, all small-for-gestational age (SGA) babies, i.e. those with birth weight lower than the 10th centile of the birth weight distribution for a given gestational age, should have the same risk of perinatal mortality. Kierans et al. (20) compared the perinatal mortality of SGA ba-

bies born in British Columbia between 1981 and 2000, belonging to four ethnic groups, i.e. Chinese, South Asian, North American Indian, and other (mainly Caucasian). When identified on the basis of a unique standard, Chinese and South Asian SGA showed a lower mortality than Caucasian SGA, whereas North American Indian presented a higher mortality. These differences tend to vanish when SGA babies were identified in accordance with ethnic-specific standards. The authors conclude, and we agree with them, that this finding "strongly suggests that the observed ethnic differences in fetal growth are physiologic, rather than pathologic, and make a strong case for ethnic-specific standards".

In addition to all these considerations, as asserted by Karlberg et al. (21), clinicians continue to prefer local references when communicating with patients and their parents, and do not take seriously any attempt to establish an international standard.

REFERENCES

1. Cameron N. A chart for all reasons. Ann Hum Biol 2009, 36: 1-4.
2. Ogden CL, Kuczmarski RJ, Flegal KM, et al. Centers for Disease Control and Prevention 2000 Growth charts for the United States: improvements to the 1977 National Center For Health Statistic version. Pediatrics 2002, 109: 45-60.
3. Grummer-Strawn LM, Ogden CL, Mei Z, et al. Scientific and practical issues in the development of the US Childhood Growth Reference. In: Martorell R, Haschke F eds. Nutrition and growth. Philadelphia: Lippincott. 2001, 21-36.
4. Sempé M, Hansson Bondallaz C, Limoni C. Growth curves in untreated Ullrich-Turner syndrome: French reference standards 1-22 years. Eur J Pediatr 1996, 155: 862-9.
5. Morison S, Dodge JA, Cole TJ, et al. Height and weight in cystic fibrosis: a cross sectional study. UK Cystic Fibrosis Survey Management Committee. Arch Dis Child 1997, 77: 497-500.
6. Clementi M, Milani S, Mammi I, Boni S, Monciotti C, Tenconi R. Neurofibromatosis type 1 growth charts. Am J Med Genet 1999, 87: 317-23.
7. Tanner JM. Growth as a mirror of the condition of society: secular trends and class distinctions. In: Demirjan A, Brault Dubuc M eds. Human growth: a multidisciplinary review. London and Philadelphia: Taylor and Francis. 1986, 3-34.
8. Gräsbeck R. The evolution of the reference value concept. Clin Chem Lab Med 2004, 42: 692-7.
9. WHO Multicentre Growth Reference Study Group. WHO child growth standards: length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: Methods and development. Geneva: World Health Organization 2006.
10. WHO Multicentre Growth Reference Study Group. WHO child growth standards based on length/height, weight and age. Acta Paediatr Suppl 2006, 450: 76-85.
11. WHO Multicentre Growth Reference Study Group. Assessment of differences in linear growth among populations in the WHO Multicentre Growth Reference Study. Acta Paediatr Suppl 2006, 450: 56-65.
12. Bertino E, Milani S, Fabris C, De Curtis M. Neonatal anthropometric charts: what they are, what they are not. Arch Dis Child Fetal Neonatal Ed 2007, 92: F7-10.
13. Ulijaszek S. Ethnic differences in patterns of human growth in stature. In: Martorell R, Haschke F eds. Nutrition and growth. Philadelphia: Lippincott. 2001, 1-20.
14. Lumey LH. Compensatory placental growth after restricted maternal nutrition in early pregnancy. Placenta 1998, 19: 105-11.
15. Júlíusson PB, Roelants M, Hoppenbrouwers K, Hauspie R, Bjerknes R. Growth of Belgian and Norwegian children compared to the WHO growth standards: prevalence below -2 and above +2 SD and the effect of breastfeeding. Arch Dis Child 2011, 96: 916-21.
16. Cacciari E, Milani S, Balsamo A, et al. Italian cross-sectional growth charts for height, weight and BMI (6-20 y). Eur J Clin Nutr 2002, 56: 171-80.
17. Cacciari E, Milani S, Balsamo A, et al. Italian cross-sectional growth charts for height, weight and BMI (2 to 20 yr). J Endocrinol Invest 2006, 29: 581-93.
18. Nicoletti I, Pelissero G. Auxologia epidemiologica e sociale. In: Nicoletti I ed. Auxologia normale e patologica, Firenze: Edizioni Centro Studi Auxologici. 1994, 611-32.
19. ISTAT. Serie Storiche. L'archivio della statistica italiana. Sanità e salute. La statura degli iscritti nelle liste di leva. http://seriestoriche.istat.it (2011).
20. Kierans WJ, Joseph KS, Luo ZC, Platt R, Wilkins R, Kramer MS. Does one size fit all? The case for ethnic-specific standards of fetal growth. BMC Pregnancy and Childbirth 2008, 8: 1-9.
21. Karlberg J, Cheung YB, Luo ZC. An update on the update of growth charts. Acta Paediatr 1999, 88: 797-802.