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Growth Assessment in Clinical Practice: Whose Growth Curve?

Howard G. Parsons · Michael A. George · Sheila M. Innis

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Abstract Differences in growth curves can influence the diagnosis of under- and overnutrition, and the interpretation of adequate growth following nutrition intervention. This effect is notable when comparing the World Health Organization (WHO) 2006 Growth Standard and the Centers for Disease Control and Prevention (CDC) 2000 Growth Reference for infants and children to 59 months of age. Important differences relate to conceptual approaches for generating growth standards to describe what population growth should be, compared to a reference of what growth is. WHO included only term infants exclusively or predominantly breast-fed beyond 4 months, and data for infants and children indicative of excess adiposity and growth failure were removed. Thus, fewer children are diagnosed with poor weight gain, and more with excess adiposity, using the WHO Growth Standard than when using the CDC Growth Reference. Adequate growth is based on proportional height and weight gains that track along growth curve trajectories. Use of the WHO curves should assist in prevention of inappropriate intervention or overfeeding in young children.

H. G. Parsons
Division of Gastroenterology, Hepatology and Nutrition,
BC Children's Hospital,
Vancouver, BC, Canada

M. A. George · S. M. Innis (✉)
Nutrition and Metabolism, Child and Family Research Institute,
Department of Paediatrics, University of British Columbia,
Room 171, 950 West 28th Avenue,
Vancouver, BC V5Z 4H4, Canada
e-mail: sinnis@interchange.ubc.ca

S. M. Innis
Division Neonatology, BC Children's Hospital,
Vancouver, BC, Canada

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Introduction

Anthropometric measurements, including weight and height or length, are an integral part of pediatric examinations and serve two key purposes. First, routine assessment of growth patterns enables the early identification of, and intervention for, children with abnormal growth due to medical, nutritional, or developmental problems [1]. Second, growth monitoring of infants and children undergoing medical care allows evaluation and adjustment of dietary intake or nutritional therapies, such as enteral and parenteral nutrition volume or composition, to better meet needs. Typically, the interpretation of anthropometric measures is aided by comparison to graphs of weight and length (or height), and their ratios plotted by age, which enables the individual child to be ranked relative to the growth and growth pattern of a group of children of the same age. The avoidance of inappropriate dietary counselling or interventions to adjust growth depends on two key points. First, the chart used for comparison should reflect the growth associated with the best short- and long-term health outcomes. Second, clinical assessment is needed of where the individual's growth potential is likely to lie relative to distribution of growth depicted in the charts.

Until recently, the growth charts most commonly used in North America were the Centers for Disease Control and Prevention (CDC) 2000 Growth References [2]. In 2006, the World Health Organization (WHO) released Growth Standards for assessment of infants and children from birth to 5 years of age [3, 4]. A WHO Growth Reference for children and adolescents 5 to 19 years of age, known as the WHO Reference 2007, was subsequently released [5]. The primary

purpose of the WHO Growth Standards was to replace the US National Center for Health Statistics (NCHS) growth reference, which since its release in 1979 has been used by numerous agencies and groups in more than 100 countries, including less-developed countries, for growth monitoring and assessment of interventions [6]. However, since the publication of the WHO Growth Standards, at least 111 countries have adopted it for assessing the growth of infants and children. In the United States, the WHO 2006 Growth Standard is recommended for assessing the growth of infants up to 2 years, whereas the CDC 2000 Growth Reference is recommended for assessing children older than 2 years [7•]. In Canada, the WHO 2006 and 2007 Growth Standard and Reference are recommended for assessing the growth of all children and adolescents to 19 years of age [8•]. This paper provides a brief review of the major differences in the CDC Growth Reference, WHO Growth Standard, and WHO Reference 2007, and then focuses on strengths and weaknesses of the CDC 2000 Growth Reference and WHO Growth Standard for monitoring the growth of infants up to 24 months of age in a clinical setting.

Background and Definitions

In practice, many physicians, dieticians, and other health care professionals likely use growth charts as standards, irrespective of how the chart was developed [7•]. An inherent assumption is that the growth chart represents an ideal or desirable norm, and allows for the appropriate identification of, and intervention for, infants and children with inadequate or excessive growth. The CDC 2000 growth charts are based on anthropometric measures of infants and children in the United States collected over the three-decade period from 1963 to 1994. Consequently, they are a description of the anthropometric measures of children in the United States over that time period; the charts are not necessarily a reflection of optimal growth at any age, and the curves are not necessarily a reflection of ideal growth patterns. The CDC growth charts are, therefore, referred to as a "Reference" because they reflect what growth was in those children at that time, not necessarily what growth should be [7•, 8•]. However, from a global perspective, an estimated 146 million children are underweight [6], whereas in 2004 an estimated 22 million children under 5 years of age and 10% of all children 5 to 17 years of age were overweight or obese, with the burden of childhood malnutrition (encompassing both under- and overnutrition) continuing to worsen [9].

From 1997 to 2003, WHO undertook a Multicentre Growth Reference Study to gather data on the growth of children from six countries (United States, Brazil, Ghana, India, Norway, and Oman) to enable generation of new growth curves for assessing the growth of infants and children around the world [3, 4]. The project was designed to overcome shortcomings of the infant portion of the NCHS Growth Reference then widely used in many countries [1, 10]. The curves were generated using longitudinal data: 21 measurements from birth to 24 months of age on about 8500 infants, birth weight greater than 1500 g, born to nonsmoking mothers, not at risk of malnutrition, and with strict inclusion criteria relating to infant feeding. The growth curves are referred to as a Growth Standard because they are considered to reflect what the growth of infants to 24 months *should* be [7•, 8•]. Infants who are breast-fed grow more quickly in the first 6 months, then more slowly to 18 months of age, than infants who are fed infant formula [11–13]. Hence, the infant feeding criteria are an important aspect of the WHO Multicentre Growth Reference Study that not only contributes to differences from the CDC 2000 charts for infants less than 24 months of age, but also impacts how healthy infant growth is viewed. In the WHO 2006 Growth Standard, all of the infants were still breast-feeding at 12 months of age, and all were exclusively or predominantly breast-fed at 4 months, with solid foods introduced by 6 months and not before 4 months of age. The CDC 2000 Growth Reference, on the other hand, had no criteria other than exclusion of infants of birth weight less than 1500 g; the infants were predominantly formula-fed, 33% were breast-fed at 3 months of age, and the measures at 2 months of age represented a small sample of 38 boys and 34 girls [7•]. Further, a primary hypothesis of the WHO study relevant to multiethnic settings was that all infants have the potential for similar growth when given appropriate nutrition. The WHO data demonstrated no difference in weight gains among infants from the six different countries [7•]. This emphasizes that the background of infants under 24 months of age is not a reason for either slow or excessive growth. It is germane to underscore that in many settings, parental weight and height may also represent neither the parents' genetic potentials nor their optimal body sizes.

A growth standard, by definition, requires removal of data for children with excess adiposity or growth failure, because the growth curves are intended to reflect the "normal" range compatible with optimum health outcomes. The WHO Growth Reference Study excluded measures for infants under 24 months of age whose weight-for-length was above or below 3 standard deviations (SD) from the median. Weight-for-length is used because it is a better indicator of unhealthy weight and avoids exclusion of healthy infants who grow more slowly or quickly from the growth distributions. The WHO Growth Standard for children 24 to 59 months of age is based on cross-sectional measures of 6669 children from the same communities that participated in the infant portion of the study, with removal of data from all boys and girls with a

weight-to-height 2 SD above or 3 SD below the median. The CDC 2000 Growth Reference for infants and children up to 59 months of age, on the other hand, excluded no "overweight" or "underweight" measurements.

WHO 2007 and CDC 2000 both provide Growth Reference curves for children 6 to 19 years of age, and both included strategies to limit an upward shift in the curves for weight and body mass index (BMI, weight [kg]/height [m^2]) because of the increasing prevalence of childhood overweight and obesity worldwide and in the United States [6, 14, 15]. Because of the difficulties of conducting large, multicenter studies in children, the WHO prepared new growth curves using existing data sets, but with the exclusion of measures suggestive of excess adiposity, with the final curves based on data for 22,917 children 5 to 19 years of age [5]. The CDC 2000 excluded all of the most recent US national survey data, the National Health and Nutrition Examination Survey III (1988–1994), for children aged 6 years and over from the growth curves as a way of avoiding an upward shift due to the increase in adiposity among US children and adolescents [8•]. The following discussion focuses primarily on infants and children up to 24 months of age, in whom differences between the CDC 2000 and WHO 2006 growth curves, differences in growth between breast-fed and formula-fed infants, and interpretation of growth measures can have a significant impact on the diagnosis of growth failure and nutrition management.

Growth Percentiles and *z* Scores

Growth charts typically describe growth of a population as a series of predefined percentiles, whereby the 50th percentile is the median of the population, and not an individual's goal. One of the dilemmas for the clinician is where an individual infant should fit on the growth curves (ie, their genetic potential for optimal growth). Thus, emphasis is typically placed on serial measures that 1) are within the lower and upper percentile boundaries of the growth chart, and 2) track along the same trajectory over time. The *z* score, also known as the SD score, although less commonly used in clinical practice, appears frequently in publications and is extensively used in population studies. The *z* score provides a measure of how far a child is from the mean or median, and hence shows the child's growth relative to the average growth of others of the same age in the population. Growth curves are available as *z* scores in addition to percentile curves, with *z* score lines of 0, +1, +2, and +3 equivalent to percentile values of 50, 84.1, 97.7, and 99.9 (rounded to 50, 85, 97, and 99) and −1, −2, and −3 equivalent to 15.9, 2.3, and 0.1 (rounded to 15, 3, and 1), respectively. Downloadable software is available (WHO Anthro, Version 2) for calculating growth percentiles and *z* scores for all measures [16]. Downloadable growth charts are also available for WHO 2006 Growth Standards and CDC Growth References in the United States [17], which are recommended in the United States for children up to 24 months and over 24 months of age, respectively [7•], and for the WHO 2006 Growth Standard and WHO 2007 Growth Reference charts [18], which are recommended for assessing the growth of all individuals up to 19 years of age in Canada [8•].

Interpretation of Individual and Serial Growth Measures and Recommended Cut-offs

As introduced, growth charts are widely used by health practitioners to assist in identification of infants and children with growth failure or excess, and for monitoring growth in response to nutritional interventions or other aspects of medical care. The assessment of under- and overweight using the CDC growth charts has traditionally been based on a weight below or above the 5th and 95th percentile values, respectively, with growth stunting identified as a length or height below the 5th percentile. The respective cut-offs using the WHO 2006 growth charts are the 3rd and 97th percentiles [7•, 8•]. The recommended cut-off is a measure below the 3rd percentile, with underweight assessed as weight-for-age, stunting as length- or height-for-age, and wasting as weight-for-length for infants to 2 years, and BMI for children 2 to 5 years of age [8•]. Because the 3rd percentile is about −2 SD, this is equivalent to a measure below −2 *z* scores on the *z*-scores charts. Infants and children meeting the definition of underweight, stunting, or wasting, therefore, have measures that fall below the lowest line on the respective WHO growth chart (Fig. 1). The assessment of excess weight gain is based on proportional growth, not body weight alone, and is assessed as weight-to-length or height for infants up to 24 months and BMI for children over 2 years of age. The recommended cut-offs for risk-of-overweight, overweight, and obesity are greater than 85th, greater than 97th, and greater than 99th percentile (equivalent to +1, +2, +3 *z* scores), respectively, with greater than 97th rather than greater than 95th percentile used as the cut-off for obesity on the Growth Reference for children and adolescents aged 5 to 19 years [8•]. The highest percentile line on the WHO growth charts is 97. As for underweight, children who fit the classification of obesity are "off" the chart and have a weight-to-height or BMI *z* score greater than 2 SD above the median.

Serial measures that cross two major percentile lines on the growth charts are often used to signal growth failure or excess, but this has inherent problems for assessment of

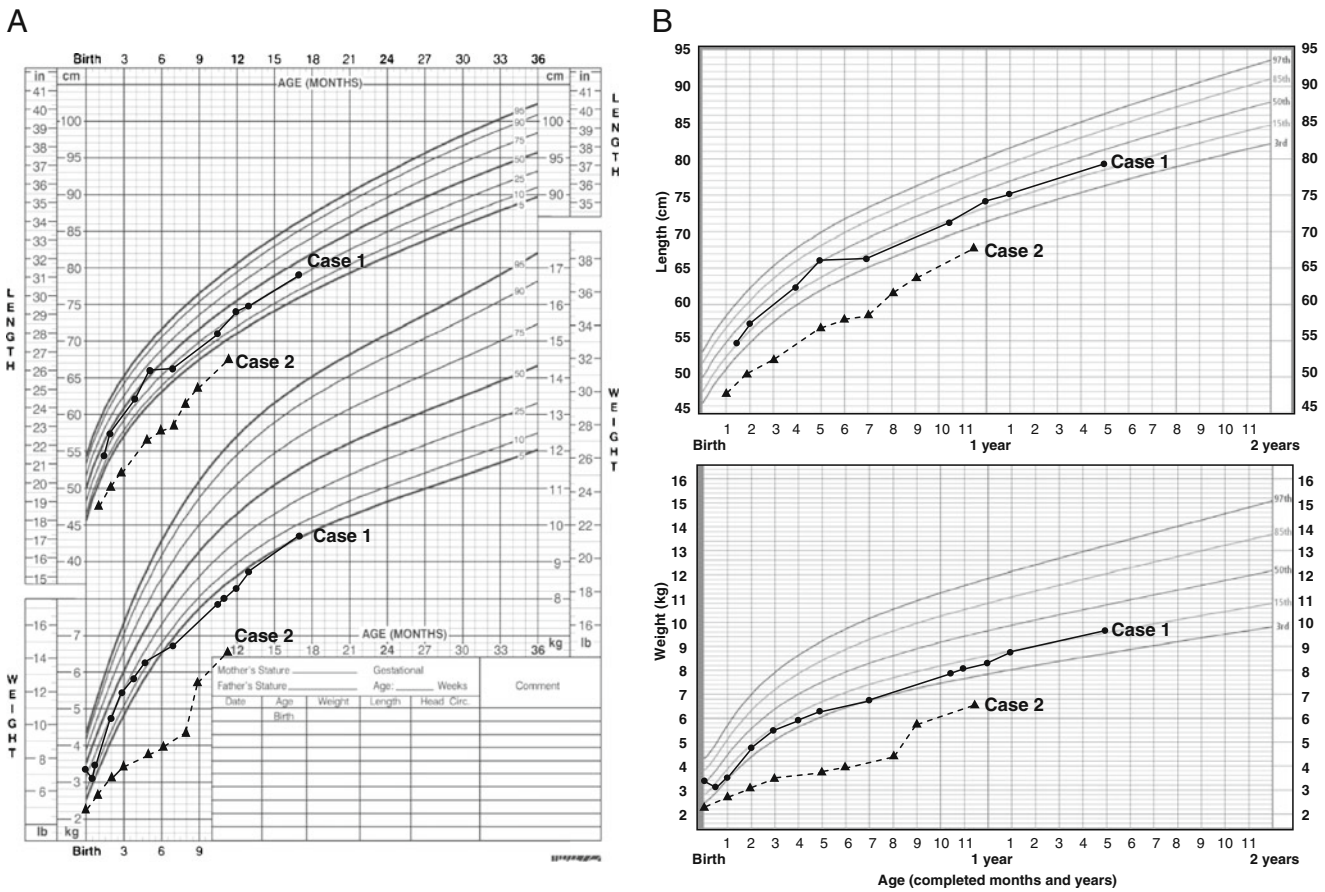

Fig. 1 The weight-for-age and length-for-age of two infants are plotted using the Centers for Disease Control and Prevention (CDC) 2000 and World Health Organization (WHO) 2006 growth curves. Case 1 illustrates a breast-fed infant diagnosed with failure-to-thrive at 7 months of age based on the CDC chart. Case 2 is a term-gestation, low-birth-weight infant diagnosed with undernutrition and stunting

infants under 24 months regardless of the chart used, and is not recommended when using the WHO 2006 [8•]. Although the percentile lines on the WHO charts are farther apart (3rd, 15th, 50th, 85th, 97th) than on the CDC charts (10th, 25th, 50th, 75th, 90th), in practice this distinction has little meaning. The infants in the WHO Growth Reference Study were more homogeneous with respect to feeding, and, in contrast to the CDC Growth Reference, data for infants with weight-to-length measurements 3 SD above or below the median were removed, giving a tighter distribution. Crossing two major percentile lines on the growth charts signifies substantial losses or gain in growth; hence infants showing such unexpected growth faltering should be investigated.

The greater problems in infant growth assessment using the growth charts relate to differences in growth between breast-fed and formula-fed infants and bumpy growth patterns of even the healthiest of infants. Because formula-fed infants grow more slowly than breast-fed infants in the first 3 months, then more rapidly than breast-fed infants from 6 to 18 months of age [11], serial measures of breast-fed infants show substantial deviations from the growth curve trajectories when plotted on the CDC growth curves [10, 12, 13]. A major shift is typically seen around 5 to 7 months of age, when the weight and weight-to-length of breast-fed infants appears to fall, often with a sharp downward crossing of percentiles. Using a group of breast-fed infants, this is seen as growth falling from above to below the 50th percentile. The percentiles lines, either above or below the 50th, crossed by an individual infant will depend on that infant's own position in the distribution. Education is important to avoid inappropriate diagnosis of growth failure and interventions, such as recommending formula feeding or aggressive counselling on the feeding of breast-fed infants who are in fact healthy and growing appropriately. The introduction of the WHO 2006 Growth Standard for assessing growth of term gestation infants from birth to 24 months of age in the United States and Canada will decrease this problem [7•, 8•]. However, education is now needed to assist interpretation of the growth of formula-fed infants when plotted on the WHO

2006 growth charts. Initial lower weight gains, followed by an increased weight gain velocity and crossing of percentile curves upward, cannot be interpreted as overfeeding or excess adiposity in formula-fed infants. The problem is illustrated by a recent analysis of 37,964 length and weight measures from 10,844 children under 24 months of age who participated in the California Growth Study conducted from 1959 to 1967, comparing the proportion of infants who crossed two major percentile lines on the CDC 2000 growth charts with the percentage who crossed corresponding lines on the WHO 2006 growth charts [19]. Breast-feeding rates in 1965 in the United States were under 30% [20], so the analysis examined predominantly formula-fed infants, plotting them on the CDC Growth Reference based on infants fed in a similar way, and on a Growth Standard based on breast-fed infants. As expected, the results suggest that pediatricians would identify more formula-fed infants less than 6 months, and fewer infants 6 to 12 months of age, as having failure-to-thrive when using the WHO 2006 growth charts. Similarly, based on re-analyzing available growth data on US children, the CDC 2000 reference indicates 7% to 11% of infants have low weight-for-age at 6 to 23 months of age, whereas less than 3% fall below the 3rd percentile on the WHO weight-for-age curve [7•]. The key message is that the lower weight and weight-for-age of breast-fed infants from 6 months of age is normal, and produces a downward shift in the growth curves. This awareness should alleviate inappropriate pressure for overfeeding of young infants. The interpretation of higher weight gains of older formula-fed infants, on the other hand, is unclear; there is no evidence that what may now appear in some such infants as an increased weight gain velocity from 6 months of age is pathological or requires intervention.

Both CDC and WHO used statistical approaches, although somewhat different, to produce smooth growth curves [4, 7•]. Infants, on the other hand, provide the growth assessor with inconvenient spurts and troughs in growth velocity. Individual measures within a series need to be considered as possibly reflecting growth spurts or troughs, which can lead to artificial shifts across percentiles. Growth percentile "surfing" is a real [8•], albeit annoying, fact of healthy growth among infants under 24 months of age and in children during puberty. Three, not two, serial measures assist in assessing the average individual growth patterns and in avoiding misdiagnosis of growth faltering based on an incidental measurement during a growth peak.

The WHO 2006 Growth Standard in Clinical Practice

The weight and length gains of two infants plotted on the CDC 2000 and WHO 2006 weight-for-age and length-for-age curves are shown (Fig. 1). Case 1 is an infant diagnosed with growth failure, and illustrates how the growth reference curve and interpretation of the measures can impact the assessment of growth and the drive for nutrition intervention. The infant was seen by consultation in gastroenterology at 13 months of age, with a provisional diagnosis of growth failure that had been made at 7 months of age, and specks of blood in his stools. The infant had been followed from early in life because of a family history of chronic renal disease, although no clinical or biochemical evidence of kidney disease was present in the infant at any time. He was developmentally normal. The infant was exclusively breast-fed for the first 6 months after birth, with the introduction of solid foods at 6 months of age, and continued breast-feeding until the current age. Concern was raised when his weight-for-age crossed two percentile lines on the CDC Growth Reference, from just above the 10th at 5 months to below the 5th percentile at 7 months of age, which led to the diagnosis of undernutrition. The early more rapid, then later slower, growth that is typical of breast-fed infants is evident. The parents were counselled on repeated occasions on techniques and foods to improve the infant's oral intake, yet despite best efforts, growth continued on a similar trajectory throughout the remainder of the first year. When seen by gastroenterology, the growth data were replotted on the WHO Growth Standard. The weight-for-age from 1 to 7 months of age runs along the 3rd to 15th percentile channel, with proportional gains in length-for-age. Weight did not fall below the 3rd percentile. The length-for-age at 5 months "surfed" to the 50th percentile, but at 7 months (when the diagnosis of failure-to-thrive was made) had returned to close to the 15th percentile, giving the impression of growth faltering. With the correct interpretation of growth using the WHO charts, the clinical support staff removed their need to pressure the parents on feeding issues. The blood in the stool was cause by a rectal fissure. The child was seen again 6 months later, at 17 months of age, when he continued to track close to the 15th percentile on the growth curves, with a noted improved relationship between the clinical staff and parents.

Case 2 shown in Fig. 1 is a boy born after 40 weeks' gestation, but with a low birth weight of 2.1 kg. The infant presented early in life with failure-to-thrive and neonatal cholestasis. For the first 6 months after birth, he was breast-fed, with the introduction of solid foods at 5 months. When seen at 7 months of age, a diagnosis of poor oral intake and failure-to-thrive led to the insertion of a nasogastric tube, with oral feeds occurring during the day and 10 h of continuous feeds provided overnight. Weight gain commenced promptly with enteral nutrition support (Fig. 1). At the same time, his cholestasis gradually resolved and solid food intake improved. The z scores for weight-for-age and length-for-age fell below the lower limit of the CDC 2000 curves of −2 SD and the WHO 2006 curves of −3 SD, accompanied by percentile values also below the curves at 7

and 11.5 months of age, giving a diagnosis of undernutrition and stunting. However, the extent of undernutrition on the weight-for-age chart at 11.5 months of age is less on the WHO 2006 than on the CDC 2000, on which the respective lower percentile cut-offs are 7.8 and 8.6 kg. The appropriate rate of catch-up growth in small-for-gestational-age term infants is unknown, and concern has been raised that aggressive nutrition with rapid weight gain will promote excess adiposity and later increased risk of metabolic syndrome [21, 22]. Extrapolation along the weight-for-age growth trajectory suggests the infant will reach the 3rd percentile of the WHO curve, thus reaching the normal range, at about 18 months of age, but not until about 28 months of age on the CDC 2000 growth curve. The potential for more aggressive feeding using the CDC 2000 growth curves in managing infants with growth failure should be apparent.

Conclusions

Growth charts, irrespective of the data on which they are based, are often used as standards to assist in identifying infants at risk of under- and overnutrition, and as tools for monitoring the adequacy of enteral and parenteral nutrition support. The WHO 2006 growth charts are recommended for assessing the growth of term infants in the United States and Canada, with cut-off values for abnormal or unhealthy growth of less than 3rd or greater than 97th percentile, or ±2 SD *z* scores, rather than the 5th and 95th percentiles, as used in the CDC 2000 growth charts. The 50th percentile represents the median growth, not an individual goal. All values within the upper and lower percentile and *z* scores lines are in the normal range. When smoothed over time, most infants and children follow the same growth curve trajectory. Individual measures can shift by one or two major percentile lines because infant growth occurs in spurts. Two major percentile lines represent substantial differences in weight and weight-for-height. Weight loss or unexplained lack of weight gain should be promptly followed up. Fewer children over 4 to 6 months of age are identified as underweight, using the WHO growth charts. When assessing formula-fed infants, their typical lower weights in the first 3 months, then heavier weights after 6 months, need to be considered in order to avoid inappropriate counselling to reduce formula or food intake. The WHO 2006 growth chart may assist in limiting unnecessarily aggressive nutritional support to promote growth in underweight infants.

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