

***Professor C C De Silva Memorial Oration - 2022***

## **Do we need to re-think growth assessment in Sri Lankan children from birth to 2 years?**

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President, Members of the Council, Past Presidents of the Sri Lanka College of Paediatricians, Members of the Family of Professor C. C. de Silva, Distinguished Invitees, Ladies and Gentlemen. I consider this as an honour and privilege to be able to deliver this year's Professor C. C. de Silva oration and I thank the President and the Council for giving me this opportunity. I dedicate this oration to Professor Percival Cholmondeley Chalmers de Silva who served this country as the first Professor of Paediatrics for 17 long years from 1949. Professor C. C. de Silva was born on the 25<sup>th</sup> of February, 1904 and was educated at St Thomas College, Mount Lavinia. After one year at the Ceylon Medical College, he proceeded to University College London, United Kingdom, where he passed the MBBS (London) and later the same year, the MRCP (London) examination, truly a Herculean feat, after which he obtained his MD (London) in 1938. In 1949, he was appointed as the Chair of Paediatrics in the University of Ceylon, which he adorned for 17 years. He established the first teaching unit at the Lady Ridgeway Hospital. In 1956, he was conferred the FRCP (London) by the Royal College of Physicians.

Professor C. C. de Silva was a pioneer in promoting breastfeeding and nutrition. In 1954, he established the Talagolla Convalescent Home for malnourished children from Ridgeway Hospital. In 1956, he established a malnutrition clinic at the Lady Ridgeway Hospital. The booklet 'Mother your baby' was jointly authored by Professor C. C. de Silva and

Mrs. N. Visvanathan. Professor C. C. de Silva also pioneered home visiting and family planning. He served as President of the Ceylon Paediatric Association from 1955 to 1957, President of the Ceylon Association for the Advancement of Science in 1961 and founder President of the Sri Lanka Nutrition Society in 1975. Professor C. C. de Silva was a prolific writer and his publications in national and international journals are plentiful. He was well-versed in music, art and literature. "Out steps the Don" and "Life as I lived it" are two of his non-medical literary works. He passed away peacefully on the 20<sup>th</sup> of May 1987, soon after he completed his autobiography. Although I was not privileged to meet or be taught by Professor C. C. de Silva, I was guided by those who had the privilege of studying under him. I hope the work I present here will be a tribute to him as Professor C. C. de Silva had a keen interest in community paediatrics and nutrition.

### **Introduction**

Regular growth assessment in children from birth to 5 years is one of many strengths of the Sri Lankan healthcare system. Growth assessment is conducted by measuring the weight and length, which are interpreted using the World Health Organisation (WHO) growth charts. Despite improvement in breastfeeding and complementary feeding indicators, in addition to an increase in the gross domestic product from 2006 to 2016, indicators for undernutrition such as stunting, wasting and underweight have been stagnant, while the percentage of obesity has been on the rise<sup>1</sup>. It is interesting to note that all these nutritional indicators are based solely on weight and/or length. This makes us question if the measurement of weight and length gives a true reflection of the nutritional status. To answer this question, I would like to use the Y-Y paradox published by Professors Yajnik and Yudkin, which demonstrated different percentages of body fat despite having the same body mass index (BMI)<sup>2</sup>. Studies conducted in Sri Lankan children aged 5-15 years have shown that BMI is a poor indicator of fat percentage<sup>3</sup>, that WHO BMI cut-offs were not sensitive enough to detect obesity in Sri Lankan children compared to locally developed BMI cut-offs that showed higher sensitivity and specificity<sup>4</sup>,

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and that the metabolic syndrome was present in boys with 28.6% fat and girls with 33.7% fat<sup>5</sup>.

This begs the question as to how early obesity originates. The insight into this question was provided by David Barker in 1986, where he described that those with intrauterine growth restriction had a higher risk of chronic disease in later life in his Early Origins Hypothesis<sup>6</sup>. This was complemented by the work done by Athul Singhal in 2004, who demonstrated the increased risk of cardiovascular disease in those with rapid postnatal growth<sup>7</sup> and by Alan Lucas in 2005, who demonstrated that poor nutrition during the first few months of life led to an increased risk of cardiovascular and bone disease as well as cognitive impairment<sup>8</sup>. These findings from Developmental Origins of Health and Disease (DOHaD) led to the understanding of the importance of the first 1000 days of life, being the ideal time for early intervention due to developmental plasticity.

This brings us to the question as to what would be the best way to assess the fat percentage in the first 1000 days of life. German chemist, Justus von Liebig (1803–1873) marked the beginning of the modern study of human body composition<sup>9</sup>. The simplest model used to describe body composition is the 2-component model where the total body weight is described using fat mass (FM) and fat-free mass (FFM). This method requires only one component to be measured, the other being determined by subtracting the measured component from the total body weight. FM can be determined by measuring the total body density using underwater weighting or air displacement plethysmography (ADP) of which only ADP is suitable for infants. FFM is determined by subtracting FM from total body weight. FFM can be determined by assessing the content of total body water (TBW) using the Deuterium Dilution (DD) technique. Here, FM is determined by subtracting FFM from TBW. Higher component models are based on measuring the components of FFM in addition to measuring FM, where measurement of TBW using the DD method in addition to FM via ADP constitutes the 3-component model and measurement of the bone mineral content (BMC) using DEXA scanning, in addition to TBW via DD and FM via ADP constitutes the 4-component model<sup>10</sup>. Existing data on body composition in Sri Lankan children are limited to cross-sectional data in infants in the first 6 months of life and children aged 5-15 years<sup>11,12</sup>. This lack of data on body composition in the first 1000 days led us to undertake the assessment of body composition of healthy infants from birth to 2 years of age.

While many factors such as sex, birth weight, maturity, age, growth velocity, parental factors,

placental factors, cord blood adipokines and growth factors, as well as infant and young child feeding (IYCF) practices, affect body composition, body composition in turn affects infant behaviour and infant development<sup>13-35</sup>. This led us to study the association of body composition with sex, birth weight, parental factors, placental factors, cord blood factors, IYCF practices, infant behaviour and infant development.

## Method

A prospective, longitudinal, cohort study was carried out in healthy infants fed according to the IYCF guidelines from birth to 2 years. Anthropometry was assessed monthly during the first year and 2-monthly during the second year. Body composition was assessed 3-monthly during the first year and 6-monthly during the second year. The relationships between body composition and feeding practices, parental factors, placental factors, cord blood factors and infant development were explored. This was the first longitudinal study on anthropometry, body composition, infant development and IYCF practices from birth to 2 years in Sri Lanka. This study was also part of the first global longitudinal body composition study, funded by the International Atomic Energy Agency which included Australia, Brazil, India, Pakistan and South Africa in addition to Sri Lanka. This study was conducted at the University Unit of De Soysa Hospital for Women, Sri Lanka from 01.07.2015 to 31.12.2019. The sample size was calculated as 150 with a power of 90% to detect FM and FFM<sup>36</sup>. Ethics approval was obtained from the Faculty of Medicine, University of Colombo (EC-14-145).

All pregnant women admitted to the university obstetric ward at a period of gestation from 37 to 41+6 weeks i.e., term gestation, were screened twice daily on all weekdays. All healthy babies born to women admitted to the University obstetric wards at term gestation, with a singleton pregnancy, aged over 18 years, living in the Colombo district, who were not smoking and had the intention to breastfeed with an income above 1<sup>st</sup> quintile according to the 2006/2007 census data and agreed to attend follow-up one-monthly during the first year and two-monthly during the second year, were included in the study. Women not fulfilling inclusion criteria were excluded. Infants with congenital abnormalities, disease conditions affecting growth, illness requiring hospital admission or an Apgar score <8 at 5 minutes were also excluded from the study.

Data were collected using interviewer-administered questionnaires and data-recording forms. English questionnaires were translated and back-translated into Sinhala and Tamil and were pre-tested on 25 infants. Questionnaires were administered in the

language of the parent's choice where separate questionnaires were used for screening and birth anthropometry, parental information, infant follow-up, 24-hour dietary recall and food frequency.

Period of gestation (POG) was assessed using crown rump length measured via antenatal ultrasound scan done between 8-13 weeks of period of amenorrhea as per national standard. In case of non-availability, biparietal diameter, measured by antenatal ultrasound, done between 13-20 weeks, was used. The last regular menstrual period of the mother was used to assess POG when both these options were not available.

Anthropometry was performed by me in all study participants following training and certification by the International Society for the Advancement of Kinanthropometry (ISAK) as a Level 2 accredited anthropometrist according to the WHO-Multicentre Growth Reference Study (MGRS) protocol<sup>37</sup>. The second measurements were performed by research assistants trained by me. The father's anthropometry and mother's height were measured at recruitment, while the mother's pre-pregnancy weight was obtained from the pregnancy record. Measurements at birth were made within the first 12-24 hours. Measurements of weight, length, circumferences (chest, abdomen, mid-arm, head) and skinfold thickness (biceps, triceps, subscapular, supra iliac) in the infant, parents' weights and heights were measured to the nearest 5g, 1mm, 1mm and 0.2 mm, 100g and 0.1cm respectively. All measurements were done using Seca GmbH instruments except for the Harpenden skinfold caliper according to the WHO-MGRS protocol<sup>37</sup>. Quality control was ensured using the same criteria used for INTERGROWTH 21<sup>38</sup>. Instruments were calibrated twice weekly. Placental weight was measured using the same instruments to the nearest 5g whereas the maximal diameter and maximal thickness were measured using a stainless-steel ruler.

Dietary data were collected using 24-hour dietary recall, food frequency and interviewer-administered questionnaires. Individual dietary counselling was done regarding the dietary components, consistency, timing of meals/ water/ breastfeeds, mealtime behaviour and interpretation of the growth curves. A mutually agreed plan was documented in the infant's clinic book in the preferred language at each visit and was followed up by myself. All participants' parents were given access to a 24-hour hotline to obtain advice regarding diet/breastfeeding. IYCF practices of the study participants were assessed using 2021 UNICEF/WHO guidelines and the 2007 Sri Lankan Ministry of Health guideline<sup>39,40</sup>.

Bio-impedance analysis (BIA) was conducted using Impedimed SBF7 with an 800µA electric current.

Tetra polar bio-impedance was assessed using dual tab manufacturer-provided electrodes with adhesive gel placed 5cm apart, with extended arms and legs, free of contact with the surroundings after keeping the baby supine for a minimum of 5 minutes, without the feet touching each other or the bed frame, following the removal of socks and all accessories including jewellery. Resistance was measured at 50kHz and 100 kHz using single-frequency BIA. Quality control was ensured by daily calibration using the RRC cell.

Deuterium oxide (D, 99.9%) was administered at 0.1g/kg at 3, 6, 9, 12, 18 and 24 months. The administered dose was calculated by determining the difference in weight between the pre- and post-administration weights of the syringe containing the dose using a 5-stage Shimadzu analytical balance<sup>41</sup>. Saliva samples were obtained using cotton swabs in screw-capped Nunc vials prior to dosing as well as 2.5 and 3 hours after dosing and stored at -20°C. Samples were analysed using Agilent Fourier-transform infrared (FTIR) spectroscopy using Micro-Lab software<sup>42</sup>. Multiple methods including testing samples in duplicate were used to ensure strict quality control. Enzyme-linked immunosorbent assay (ELISA) was conducted for leptin, adiponectin, insulin and IGF-1 in cord blood (10ml) that was collected at the time of birth, and stored at -80°C after centrifuging.

I also conducted Bayley III assessments on all participants at 3, 6, 9, 12, 18 and 24 months in the family's language of choice, where raw scores were recorded for all domains. Scaled scores and growth scores were derived from raw scores, whereas composite scores were derived from scaled scores.

Statistical analysis was done using SPSS version 27 for Mac. Data cleaning was performed using box and whisker plots for cross-sectional data and 'plot clean' and 'velout' functions using Sitar on R studio. The normality of the distribution was checked using the Shapiro-Wilk test. Z-scores were determined using the WHO Anthro analyser for MacBook. Longitudinal curves and percentiles were determined via LMS chart maker. Relationships between variables were determined using the independent sample t-test, Pearson and Spearman correlation and simple, multiple and hierarchical linear regression after satisfying all assumptions. Age at each visit was calculated using the visit date and the date of birth. A 30-day period was taken as a month.

## Results

The total screened was 4140, of which 877 were eligible; of this, 427 consented and were recruited prior to delivery, but only 344 consented after delivery. Seven babies were excluded due to birth

records not being available resulting in a study population of 337 at birth. Study population was 157, 122, 76, 44 and 36 at 1, 3, 6, 12, 18 and 24 months of age. Socio demographic data were similar

to that obtained from national surveys as shown in Table 1.

**Table 1: Comparison of sociodemographic data of our study population to national data (n=337)**

Characteristic	Maternal	HIES 2016	Paternal	HIES 2016
<i>Education: n (%)</i>				
Not attended school	04 (01.1)	03.3%	05 (01.4)	03.4%
Primary	12 (03.6)	23.5%	57 (17.0)	21.8%
Secondary	302 (89.7)	70.5%	260 (77.3)	71.8%
University	06 (01.7)	02.7%	07 (02.0)	02.9%
Professional	13 (03.9)	-	08 (02.3)	-
<i>Occupation: n (%)</i>				
Housewife	208 (61.7)	64.4%**	05 (0.9)	25.1%**
Skilled manual work	82 (24.4)	22.4%**	195 (57.8)	21.0%**
Unskilled manual work	07 (02.2)	19.9%**	02 (0.6)	19.4%**
Managerial	31 (09.2)	13.2%**	85 (25.2)	14.3%**
Clerical support	09 (02.5)	06.3%**	52 (15.5)	03.5%**
<i>Age: Mean <math>\pm</math> SD (Range)</i>	29 $\pm$ 6 (19-44)	28.8*	32 $\pm$ 6 (19-52)	31 $\pm$ 6 .3***

HIES: Household Income and expenditure survey 2016<sup>43</sup>, \*Sathees et al 2021<sup>44</sup>, \*\* Sri Lanka labour survey 2012<sup>45</sup>, \*\*\* Mahesh et al 2006<sup>46</sup>

Table 2 is a comparison of the sociodemographic data of our study population to national data. Although our study population had a lower income,

ownership of commodities was higher in our study population compared to the national data (Table 2).

**Table 2: Comparison of sociodemographic data of our study population to national data**

Characteristic	Study data	HIES 2016 <sup>47</sup>
<i>Income</i>		
Median (Inter quartile range)	30,000 (25,000-45,000)	43,511
1 <sup>st</sup> quintile (Less than 23,518): n (%)	75 (22.4)	04.8%
2 <sup>nd</sup> quintile (23,519 – 36,445): n (%)	144 (42.7)	19.6%
3 <sup>rd</sup> quintile (36,446 – 51,862): n (%)	65 (19.3)	14.0%
4 <sup>th</sup> quintile (51,863 – 81,371): n (%)	33 (09.7)	20.7%
5 <sup>th</sup> quintile (81,371 upwards): n (%)	20 (05.9)	50.8%
<i>Ownership</i>		
Safe drinking water	100%	88.8%
Own flush toilet	100%	91.7%
Refrigerator	71.6%	52.9%
Gas/Electric cooker	86.1%	53.9%
Telephone	99.1%	91.5%
Car	12.7%	09.3%

HIES: Household Income and expenditure survey

During the first 7 months of life, exclusive breastfeeding (EBF) was the predominant method of feeding, although it showed a gradual decrease from 100% to 90% from birth to 4 months of age. Predominant breastfeeding increased from 2-14% from 1 to 7 months of age. Formula feeding was 1-3% where the duration of formula feeds was less than one month in all babies who either converted to EBF or solid and semisolids. None of the babies received unmodified animal milk during this period; 82% initiated solids and semisolids between 6-8 months of age, whereas 18% initiated earlier at 4-6 months of age as advised by the investigator (82% due to flattening or faltering in the weight for age growth curve on the CHDR)<sup>48</sup>.

While almost all babies (96%) continued to breastfeed till the end of the first year, only 75% were breastfed at the end of 2 years. Consumption of grains was 100% whereas that of vegetables and fruits, especially those rich in vitamin A, was 90-100% at all ages. Flesh food consumption increased with age, from about 55% at 6 months to 90% at 8 months. Consumption of pulses was 40-60% at all ages, compared to eggs which increased from 15% to 50-60% from 6 to 12 months of age. Consumption of dairy food, other than breastmilk, i.e., mainly yoghurt and cheese, increased from 19% to 70-80% from 5 months to one year<sup>48</sup>.

Our study population had very high adherence to 2021 UNICEF / WHO guidelines where minimum dietary diversity, minimally acceptable diet, minimum meal frequency and egg and/or flesh food consumption were more than 90% from 9-24 months without sweetened beverage consumption at any age<sup>48</sup>. Our study population also had very high adherence to the latest Sri Lankan guideline on complementary feeding (2007) with more than 90% adherence to age-appropriate consistency, and responsive feeding<sup>48</sup>. Our study population demonstrated better IYCF indices than DHS 2016/2017 and achieved the proposed national targets for 2020 except for continued breastfeeding (CBF) for 2 years, most probably due to individual counselling during each visit<sup>48</sup>.

Comparison of the birth anthropometry in our Sri Lankan study population with the WHO MGRS study revealed that we had significantly ( $p < 0.05$ ) lower birth weight ( $2.9 \pm 0.4$  kg) and length ( $48.5 \pm 2.3$  cm) with significantly higher percentage of low birth weight of 16.3%, where the Z-scores for weight, length and weight for length were lower by 0.6-0.8 SD compared to the WHO MGRS<sup>49</sup>. Despite our study population also demonstrating a higher adherence to the IYCF guidelines, compared to WHO MGRS, where initiation of breastfeeding was 100% vs 66%, EBF / predominant breastfeeding was 97.8% vs 75%, breastfeeding at 12 months was 99% vs 68% and breastfeeding at 24 months was 73% vs 16%, weight, length and weight for length in our study population was 0.6-0.9 SD lower than WHO MGRS similar to the pattern seen with birth anthropometry. This results in weight, length and weight for length less than -1SD being falsely labelled as underweight, stunting and wasting resulting in an overestimation of these nutritional indicators, resulting in overfeeding to achieve the WHO growth standards, thereby increasing the risk of obesity and all its complications<sup>50</sup>.

However, it was interesting to note that the mid-upper-arm circumference and the subscapular skinfold thickness from birth to 2 years were similar or higher in our Sri Lankan study population compared to WHO MGRS. This raised the question as to whether Sri Lankan children are smaller in size with a lower weight and length but have higher adiposity. A comparison of Sri Lankan newborns in our study population with published data from other countries revealed that our study population from Sri Lanka had a significantly higher abdominal circumference despite a significantly lower weight and length, compared to Australian and Canadian neonates. Abdominal circumference has been found to have a good correlation with visceral adipose tissue and subcutaneous abdominal adipose tissue<sup>51</sup>.

Assessment of body composition during the first 2 years using the DD method revealed that FFM steadily increased with age, while FM showed an initial rapid increase during the first 6-9 months followed by a much slower increase with almost a plateau, where FM% reflected similar changes that were shown by FM<sup>52</sup>. However, the DD method is not suitable for day-to-day practice due to requiring a minimum of 3 hours as well as the need for laboratory facilities for analysis. This led us to undertake single frequency bio-impedance assessment (BIA) that can be conducted in the field setting and takes only a few minutes, for the assessment of infant body composition. Cross-validation with the DD method was done using split sample analysis. Impedance index at 100kHz demonstrated a 95% agreement with FFM using the Bland Altman plot, implying that BIA done at 100kHz from birth to 2 years can be used to predict FFM. We also found that abdominal circumference, chest circumference and the sum of skinfolds can be used to predict body composition during the first 2 years of life.

We then went on to explore the factors associated with infant body composition. Females had a higher percentage of fat despite having lower weight and length from birth to 2 years<sup>53</sup>. Small for gestational age babies were smaller in size with lower adiposity at the time of birth, but went on to show an accelerated growth rate from birth to 2 years with a rapid increase in adiposity from birth to 6 months and demonstrating the high adiposity till 2 years of age while remaining smallest in size<sup>54</sup>. Increased compliance to IYCF guidelines was seen to be associated with an increase in FFM and decrease in FM%, whereas non-adherence denoted by consumption of salt and bottle feeding was associated with an increase in the FM%. Furthermore, adherence to IYCF was seen to increase the Bayley III scores for cognition, motor and language. An increase in parental height and education as well as maternal haemoglobin were seen to increase FFM and its derivatives, whereas increase in parent weight and family income was seen to increase FM and its derivatives. We also found that an increase in placental thickness was associated with an increase in adiposity and that it could be used to predict infant adiposity at 2 years of age<sup>43</sup>. In addition, we demonstrated that cord blood adipokines and growth factors could also be used to predict infant body composition. An increase in cord insulin and adiponectin was associated with an increase in FM, whereas cord IGF-1 was associated with the increase in FFM. Cord leptin did not demonstrate an association with either FM or FFM. Considering the association of body composition with maternal factors, cord factors and placental factors, we demonstrated that increased infant fat mass was associated with increased

maternal weight at booking visit and increased placental thickness, where increased placental thickness was associated with increased cord blood leptin and insulin levels. This implies that maternal anthropometry may mediate offspring adiposity through changes in cord leptin and insulin levels and increase in placental thickness. Placenta can be used to predict body composition in infants<sup>55</sup>. Interestingly, we also demonstrated that an increase in FM% decreased Bayley III scores, whereas an increase in FFM% increased Bayley III scores.

#### Problems identified and proposed solutions

Healthy Sri Lankan infants with good adherence to IYCF are smaller in size than the WHO reference population. Therefore, growth assessment using the WHO MGRS chart overestimates wasting, stunting and underweight in our Sri Lankan population, while underestimating obesity. Hence, we need country or region-specific growth charts to represent our population, which can be easily done by re-naming the SD lines after shifting the currently used WHO-MGRS SD lines upwards by 1 SD as shown in Table 3.

**Table 3: Suggested upward shift of SD lines by one standard deviation to prepare country specific growth charts for weight and length**

Current	New
-3SD	-2SD
-2SD	-1SD
-1SD	MEDIAN
MEDIAN	+1SD
+1SD	+2SD
+2SD	+3SD

Another problem identified was the promotion of catch-up growth in small for gestational age (SGA) babies. These babies were seen to have a higher fat mass from 3–24 months despite smaller size along with accelerated growth rate with more than 0.7SD change, despite adhering to IYCF guidelines. Trying to achieve catch-up growth will further increase the growth rate and increase the risk of obesity as well as have a negative impact on development. Awareness needs to be increased about the fact that babies with higher growth rates have poor outcomes. We need to encourage babies to grow along their birth centile and stop interventions such as overfeeding and formula supplementation to achieve catch-up growth. We should also focus on primary prevention of SGA by intervening prior to pregnancy.

We also saw the importance of adhering to the IYCF guidelines, where increased adherence resulted in increased FFM and increased neurodevelopment in contrast to poor adherence which resulted in increased FM and decreased neurodevelopment. The high level of adherence to IYCF in our study

population despite having low income was thought to be due to individualized counselling and regular follow-up with documentation at every visit. We propose to revise the local IYCF guideline and circular of 2007, by recommending avoiding sugar beyond 1 year (not only during the first year), avoiding salt beyond 1 year (not only during the first year), not to engage in straining or blending food at any point, not to give biscuits as extra snacks in growth faltering, to give whole eggs from the beginning of the 7<sup>th</sup> month with other flesh foods, to structure breastfeeding after starting complementary feeds and not to recommend additional fat other than what is used for cooking e.g., coconut milk. We also propose to individualize IYCF counselling by including the family preferences, religious and cultural beliefs, lifestyle – time they wake up and go to sleep, availability of a refrigerator, occupation, feeding behaviour and adverse effects of non-adherence to IYCF. We recommend regular monthly follow-up where the impact of feeding on the growth chart should be demonstrated at each visit. We suggest documenting the agreed meal plan including the suggested time slots and re-visiting this plan at each visit and reviewing what worked and what did not, based on which, the plan could be revised with mutual agreement. We also suggest using peer learning, where experience is shared among the caregivers of different children and enables access to a 24/7 hotline to offer support with any challenges during adherence to IYCF.

Another problem identified was that of body composition not being assessed as part of the present-day growth assessment in infants. Measuring placental thickness and measuring the chest and abdominal circumferences can be used to predict body composition from birth to 2 years at no additional cost. In addition, BIA and cord blood analysis can also be used to predict body composition but would incur an additional cost.

Unawareness of the effects of parent weight and income on infant body composition was another problem that was identified. Increasing awareness about parents' obesity being transmitted to their offspring as well as how to utilize finances to increase healthy eating, healthy living and avoiding junk food is likely to help to overcome this problem.

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