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Plasma and Blood Volume Studies in Healthy Children

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Summary

Adeyokunnu AA, Antia AU and Bamgboye EA. Plasma and Blood Volume Studies in Healthy Children. *Nigerian Journal of Paediatrics* **1982; 9: 33.** Plasma and total blood volumes of 68 healthy Nigerian children, aged 1 day to 12 years, were determined by the dye haematocrit technique using Evan's blue (T 1824). The average plasma and total blood volumes in ml/kg body weight were 48.1 and 79.9, respectively. Total plasma and total blood volumes for both sexes increased steadily with age, but there was a more rapid increase during the first 4 years of life than during later ages. Compared with height and surface area, weight was the best correlative factor for the prediction of blood volume. The results were comparable with those in children elsewhere.

Introduction

RATIONAL management of several clinical states including shock, dehydration and anaemia must take into consideration, the plasma and total blood volumes of individual patients. Establishment of normal values of plasma and total blood volumes for all age groups is, therefore, of considerable clinical importance. Most previous studies on plasma and blood volumes concerned caucasian children.[1-7] To our knowledge, there have been no previous reports on plasma and blood volumes in healthy African children. The present study was carried out in order to establish the normal values of plasma and blood volumes in healthy Nigerian children and also to compare the findings with those of children elsewhere.

In the present study, the dye haematocrit technique using Evan's blue (T 1824) as a tracer was employed in preference to radioisotopes because facilities for radioisotope studies, though available here, are associated with serious problems. First, the supply of radioisotopes is irregular. Secondly, the volumetron, an instrument used for performing on-the-spot determination of blood volume, often breaks down due to constant fluctuations in electricity supply. Thirdly, because of ethical considerations, we were sceptical about the use, handling and disposal of radioisotopes on a large scale in neonates, infants and children. More importantly, many parents,

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because of real and imaginary fears about radiation were unwilling to give consent for their healthy children to be studied. Although the Evan's blue technique is outdated, it has been found reliable and nontoxic;[8] it still fulfils a role in base-line studies such as the present one.

Subjects and Methods

The subjects included newborn babies who were products of spontaneous vaginal delivery in the Obstetric Unit, University College Hospital (UCH), Ibadan, under-five children attending the Baptist Nursery School near the hospital and children above 6 years of age attending the Odinjo primary school, situated in the centre of Ibadan. Informed parental consent was obtained in each case.

All the subjects underwent physical examination to exclude those with acute illnesses such as fever, diarrhoea and vomiting; those with chronic illnesses like anaemia, enlarged spleen or liver or any evidence of other systemic diseases. The neonates and younger children were weighed without clothes and their heights measured using Tanner's table, while the older children were also weighed without clothes and their heights measured without shoes. The surface area was calculated from the formula of Du Bois and Du Bois.[9] On the morning of the investigation, the school children were collected from their respective schools to the hospital, and similar to the technique used by other workers,[1 2 3 6 7] these children, with the exception of the infants and the toddlers, were kept in bed with nothing to eat or drink from 7 a.m. to 12 noon.

Plasma volume was determined by the dye-dilution method, using Evan's blue (T 1824). The quantity of dye used varied between 0.5 mg and 0.8 mg per kg body weight. Amounts within these limits have been found to give suitable dilutions for reading on the photoelectric colorimeter.[9]

Before the dye was injected, 5-10 ml of whole venous blood was aseptically obtained from either the antecubital vein in older children or the scalp vein in the neonates and the samples were placed in sterile universal tubes containing dry heparin as anticoagulant. This dye-free specimen served as the dye pre-equilibration sample. The calculated amount of dye was then injected intravenously, care being taken to avoid spilling. Complete flushing of the dye from the side of the syringe was ensured by filling and emptying the syringe at least five times with the patient's blood. The time of injection was recorded using a stopwatch. Two post-injection venous samples were obtained at the 10th and 15th minutes respectively from the opposite antecubital vein or umbilical vein since the mixing of the dye in the blood is usually complete within 10 minutes although there may be a delay of up to 15 minutes in patients with prolonged circulation time as occur in shock or heart failure. The samples were centrifuged and the plasma pipetted off. Dye was extracted from the two dye-containing plasma samples, using the dye extraction method developed by Campbell, Frohman and Reeve.[8]

A cuvette containing the dye-free plasma was set in the spectrophotometer and the instrument adjusted to zero optical density at 620 millimicrons (mu). The dye-containing plasma samples were then inserted and their optical density at the same wavelength, recorded.

Packed cell volume or haematocrit (PCV) was determined in triplicate, on the venous blood samples using a Hawksley's microhaematocrit. By the method, no correlation was considered necessary for trapped plasma while calculating the plasma volume.[10] Haemoglobin was measured as cyamethaemoglobin with a photoelectric colorimeter.

The total plasma volume was calculated by dividing the weight of dye injected in mg by the concentration of dye in plasma at zero time in mg per ml. Total blood volume was calculated from the formula:

$$\text{Total blood volume} = \text{Total plasma volume} \times \frac{100}{100 - \text{PCV}}$$

Both the unit plasma and blood volume were derived by dividing respective total values with the subject's weight.

An IBM computer was used for data analysis and the regression/correlation equation were obtained using computer programme. Values were correlated with age, sex, weight, height, surface area and haematocrit values.

Results

There were 68 children (33 females and 35 males), aged between 1 day and 12 years.

Effect of Age: Table I shows the mean plasma and blood volumes respectively, per kg of body weight. A gradual but steady increase of plasma volume with age is evident. There was a low but positive correlation between plasma volume in ml/kg and age ($r=0.2$) which was statistically significant ($p<0.05$). The mean blood volume was high in the first year of life and low in the next three years, followed by a gradual rise from the the fourth year onwards. A poor inverse correlation of mean blood volume with age was observed ($r=0.19$). The total plasma volume gave a highly positive correlation with age ($r=0.96$; $p<0.001$). The relationship which was linear (Fig 1) is described by a predictive equation: $TPV=180.43+118A$ (where TPV=Total plasma volume and A =Age in years). Fig 2 shows that the total blood volume also gave a significantly high positive correlation ($r=0.94$; $p<0.001$). The predictive equation derived from this is: $TBV=309+189A$ (where TBV=Total blood volume and A=Age in years).

TABLE 1

Mean Plasma and Blood Volumes According to Age Group

Age (Years)	*Plasma Volume (ml/kg)*		*No of cases*	*Blood Volume (ml/kg)*		*No of cases*
	Mean	*SE*		*Mean*	*SE*	
< 1	46.64	1.14	20	86.43	3.01	20
1 – 3	46.53	1.22	6	73.32	2.32	6
4 – 8	49.75	1.05	21	79.86	1.68	21
9 – 12	49.52	1.54	21	79.94	2.67	21

Effects of Weight and Height: A significantly high correlation was observed between total plasma volume and weight ($r=0.97$; $p<0.001$), while the correlation between plasma volume and height was poor ($r=0.18$; $p<0.05$). There was an inversely linear correlation between the weight and blood volume in ml/kg body weight ($r=0.27$; $p<0.05$), but the coefficient of correlation between total blood volume was high ($r=0.97$). This relationship, which was linear (Fig. 3), was significant ($p<0.001$).

The relationship between the height and total plasma and total blood volumes are depicted in Figs. 4 and 5 respectively. The relationship of height to blood volume in ml/kg was inverse and the coefficient of correlation was poor. The regression equation (Table II) and the coefficient of correlations (Table III) for the different parameters showed a poor correlation between height and the plasma volume ($r=0.23$; $p<0.05$).

Venous Haematocrit: A linear relationship was only evident between the venous haematocrit (PCV) and blood volume (Fig. 6). There was poor correlation between it and the plasma volume.

Effect of Sex: The mean plasma volume in girls was 47.53 ml/kg and the mean blood volume 80.77 ml/kg, while the corresponding values for boys were 49.38 ml/kg and 81.73 ml/kg. There was, therefore, no significantly discernible sex difference in the values of the plasma and blood volumes.

Discussion

In the present study, the choice of methodology was dictated by available facilities as well as by the consideration for the safety of the procedures to the subjects. Evan's blue was used as

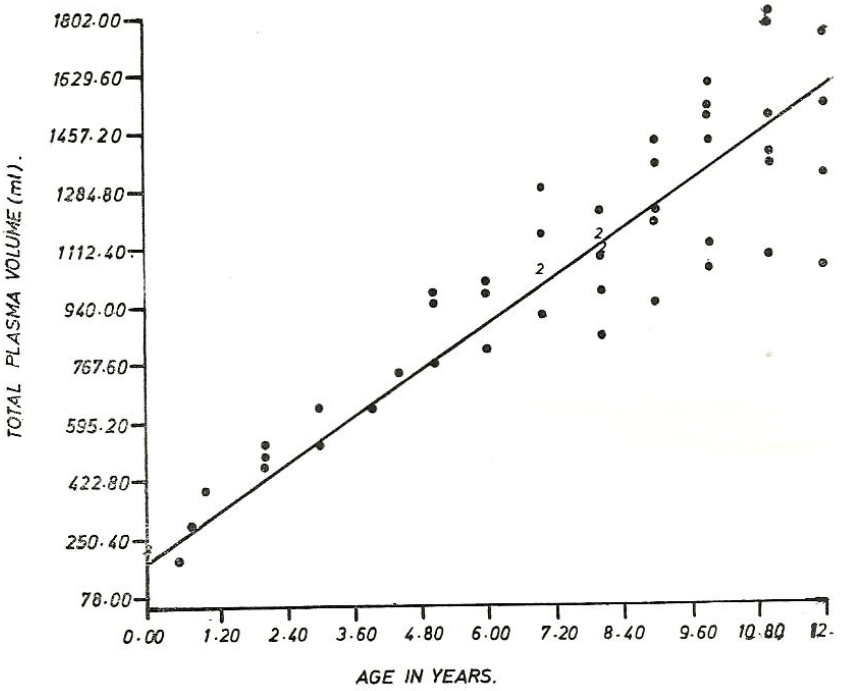

Fig. 1 Relationship between total plasma volume and age. Aggregation of patients (n= 18) in the first 33 days of life have not been scored.

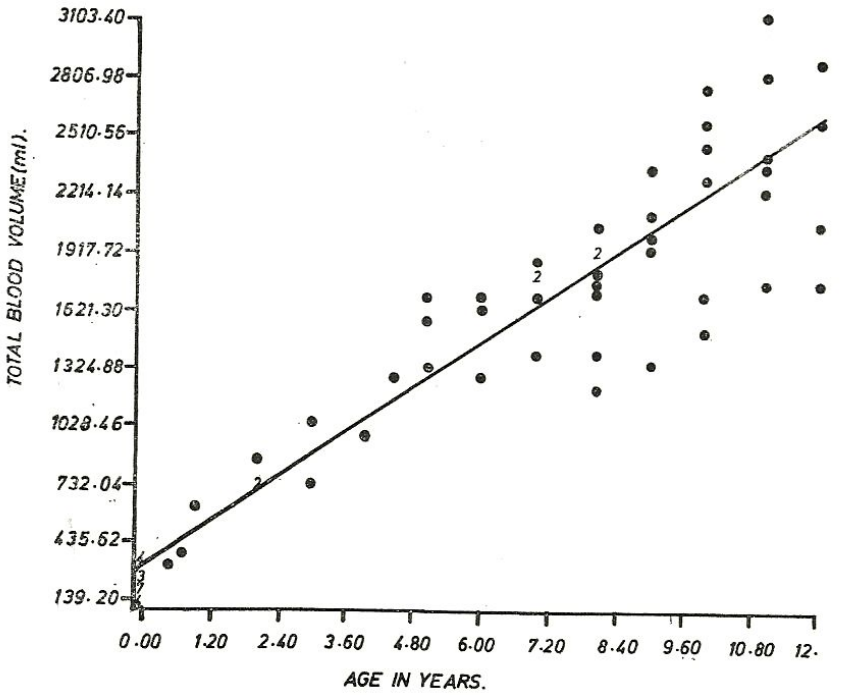

Fig. 2 Relationship between total blood volume and age. Note the scatter at about the 8th year.

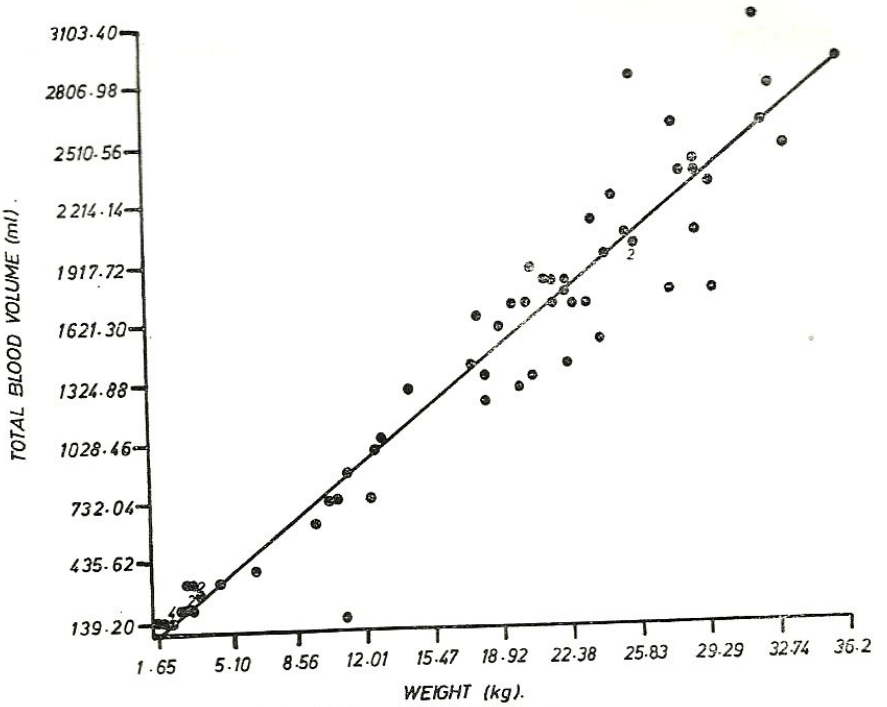

Fig. 3. Relationship between total blood volume and weight.

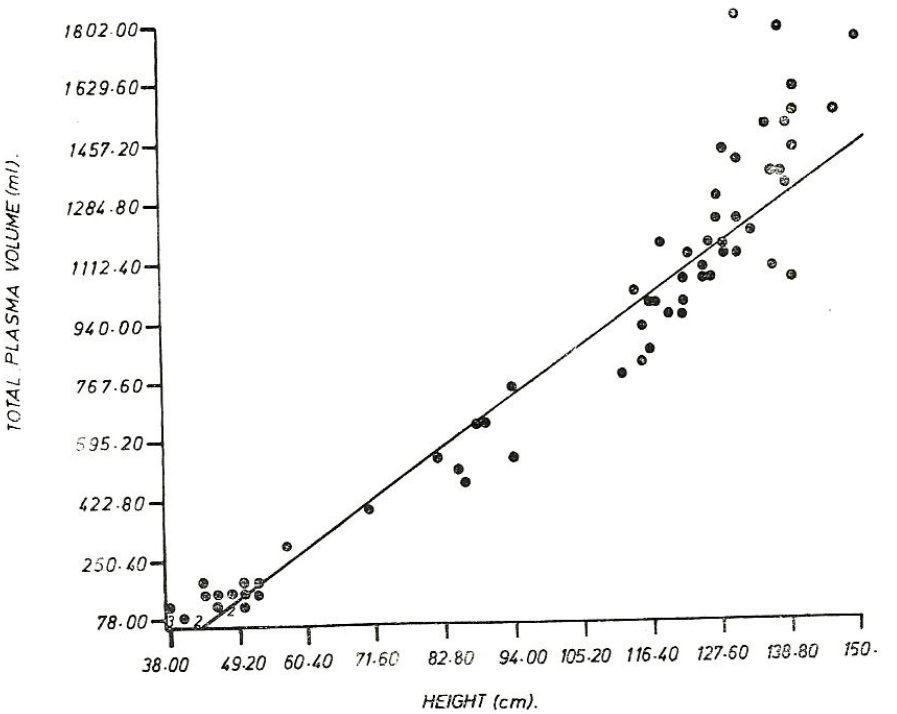

Fig. 4. Relationship between total plasma volume and heihgt

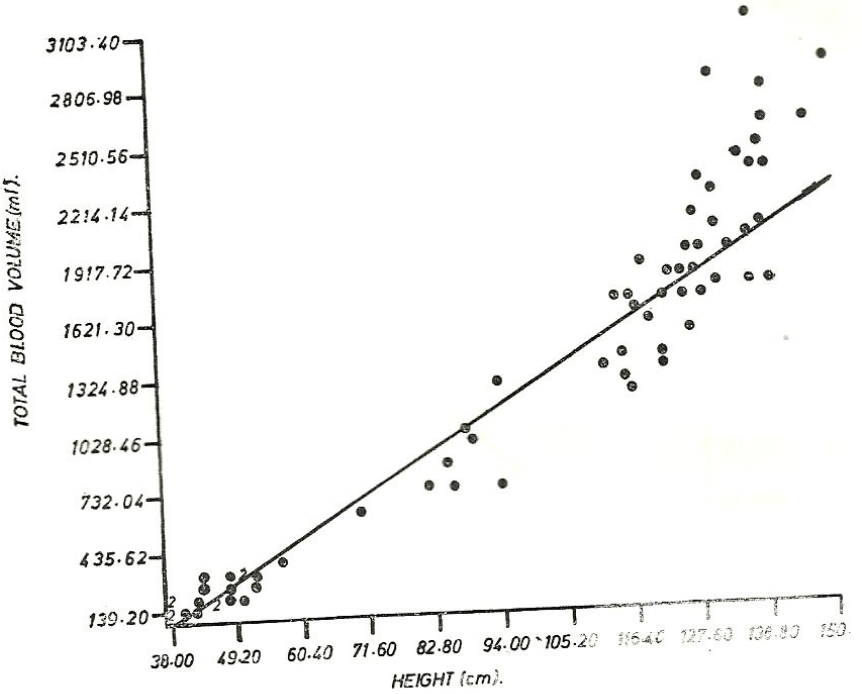

Fig. 5 Relationship between total blood volume and height.

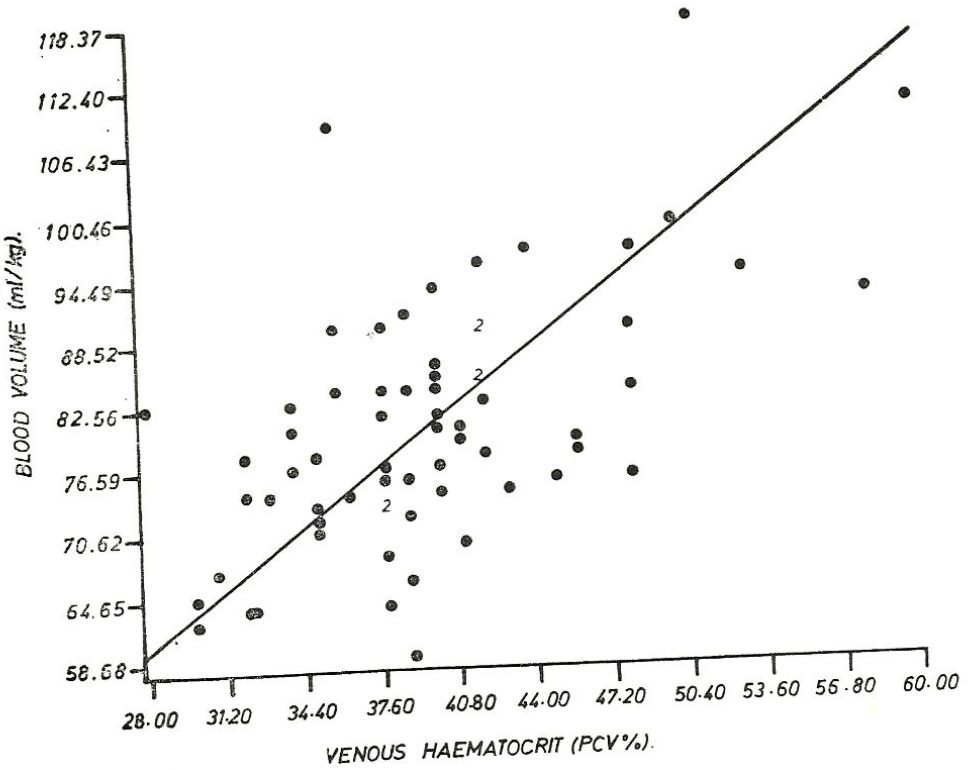

fig. 6. *Relationship between blood volume and venous haematocrit. Note the wide scatter.*

TABLE II

Regression Equations of Total Plasma and Blood Volumes (TPV and TBV) on Weight, Height and Age

	TPV	*TBV*
Weight	TPV = —17.5 + 50 Wt	TBV = —22 + 80.44 Wt
Height	TPV = —503.11 +13.4 Ht	TBV = —785 + 21.5 Ht
Age (yrs)	TPV = 180.43 + 118.12 Age	TBV = 309 + 189 Age

TABLE III

Coefficient of Correlation (r) of PV, TPV, BV, TBV with Weight, Height and Age

	PV	*TPV*	*BV*	*TBV*
Weight (wt)	0.18	0.97**	0.21**	0.97**
Height (ht)	0.23*	0.96**	0.23*	0.95**
Age (yr)	0.22*	0.96**	0.19	0.94**

PV = Plasma Volume BV = Blood Volume

TPV = Total Plasma Volume TBV=Total Blood Volume

*Shows significance at $P < 0.05$
**Shows significance at $P < 0.001$

a tracer in preference to radioisotopes in order to avoid radiation, however insignificant its risk. The errors to which the method might be subject due to plasma colour intensity, haemolysis, lipaemia and plasma colour carotene were adequately taken care of, by using the dye extraction method of Campbell *et al*.[8] We were also able to test the experimental accuracy of our method by successfully measuring accurately, a known volume of blood in a glass container. Results of the dye-dilution technique using T1824 have, moreover been found comparable to other methods using radioisotope tracers. The present results have therefore been presented and compared with the results of other workers [1 2 5 6 11] who used methods and age groups similar to ours.

Several workers have reported progressive increase in plasma and blood volumes respectively, with increasing age in childhood. [1 2 5 11] The present study has confirmed these previous reports. Although Seckel [7] has described two peak periods when the observed rise became excessive namely: ages 3-6 and 11-13 years respectively, this phenomenon was not observed in the present study. It is worthy to note that in the present study, the mean value of 86.4 ml/kg body weight obtained in infants was higher than the mean value in older children. This finding agrees with the mean values of 83.0 ml/kg body weight, 84.7 ml/kg body weight and 78.7 ml/kg body weight reported by Seckel,[7] Mollison and Cutbush[2] and Russell,[1] respectively.

The observation of Retzlaff and colleagues[12] of lower plasma and blood volumes in adult women than their male counterparts, and the confirmation of this finding in childhood by Russell,[1] led us to analyse separately, the plasma and blood volumes in the 33 females and 35 males. As shown above, there were no discernible sex differences in both plasma and blood volumes in the present series. The present findings, therefore, agree with those of Brines, Gibson and Kunkel[6] who found no difference between the sexes until puberty, when boys began to have larger blood volumes than girls of the same measurements.

In the present study, body weight as a reference parameter, gave a high positive coefficient of correlation which was comparable with those of other workers from different parts of the world (Table IV). However, an objection to the use of body weight as a correlative factor, is the fluctuation that might occur in weight in conditions like dehydration, marasmus and oedema. Because of this objection, Nadler, Hidalgo and Block[13] and Gross and Godel[14] have advocated the use of surface area of the body. It should be emphasised

TABLE IV

Summary of Plasma and Blood Volume Values by Different Workers

Investigator	*Age (Years)*	*No of cases*	*Mean Plasma Vol. (ml/kg)*	*Mean Blood Vol. (ml/kg)*
Brines *et al*[6]	0–17	50	41.8	69.8
Morse *et al*[5]	1–13	40	50.1	84.1
Mollison *et al*[2]	Newborn	9	42.6	77.1
Mollison *et al*[2]	1–12	34	59.7	84.7
Russell[1]	0–13	80	47.8	83.5
Shah[11]	0–12	31	46.9	80.2
Present series	0–12	68	48.1	79.9

that in the present study, the subjects were apparently healthy and therefore, the above objection was not applicable. Thus, weight was the most reliable parameter from which to calculate blood volume as compared with age, height, and surface area of the body. In communities where reliable development charts are available, the blood volume of an ill child may be calculated from the expected weight thereby, making allowance for fluctuations in weight during ill-health.

Acknowledgement

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