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Evaluation of the effectiveness of the national vitamin A supplementation programme among school children in Sri Lanka

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The Ministry of Health in Sri Lanka commenced a vitamin A supplementation programme of school children with a megadose of 105 µmol (100 000 IU) vitamin A in school years 1, 4 and 7 (approximately 5-, 9- and 12-year-olds, respectively) in 2001. We evaluated the vitamin A supplementation programme of school children in a rural area of Sri Lanka. A cross-sectional study was conducted among children supplemented with an oral megadose of vitamin A (105 µmol; *n* 452) and children not supplemented (controls; *n* 294) in Grades 1–5. Children were clinically examined and a sample of blood was taken for serum vitamin A concentration estimation by HPLC. Socio-demographic information was obtained from children or mothers. Supplemented children had a higher proportion of males and stunted children, were younger and lived under poorer conditions as compared to controls. There was no difference in the prevalences of eye signs and symptoms of vitamin A deficiency in the two groups. Supplemented children had higher serum vitamin A concentrations than controls (1·4 (SD 0·49) µmol/l *v.* 1·2 (SD 0·52) µmol/l). The serum vitamin A concentrations were 1·6 (SD 0·45), 1·4 (SD 0·50), 1·3 (SD 0·44) and 1·1 (SD 0·43) µmol/l in children supplemented within 1, 1–6, 7–12 and 13–18 months of supplementation, respectively. Vitamin A concentrations were significantly greater than controls if supplementation was carried out within 6 months after adjustment. The oral megadose of 105 µmol vitamin A maintained serum vitamin A concentrations for 6 months in school children.

Vitamin A supplementation: School children: Oral megadose: Vitamin A concentrations: Sri Lanka

Vitamin A deficiency is a significant public health problem throughout the world, affecting millions of school children. Among the proposed strategies to correct the deficiency, the distribution of capsules containing a high dose of preformed vitamin A to at-risk populations is practised and supported widely by international organizations due to its immediate impact and the possibility of it being implemented via the existing health care infrastructure (Sommer, 1989).

Vitamin A deficiency is a public health problem in Sri Lanka (Medical Research Institute, 1998). The Government of Sri Lanka in its national plan of action aimed to achieve virtual elimination of vitamin A deficiency and its consequences (Nutrition Division, 1999). The current national programme of vitamin A supplementation, commenced in 2001, includes using an oral megadose of 210 µmol (200 000 IU) for postpartum mothers within 4 weeks of delivery, and 105 µmol (100 000 IU) for infants at 9 months with measles immunization, preschool children at 18 months with oral polio vaccine and diphtheria, pertussis and tetanus immunization, and school children in Grades 1, 4 and 7 (approximately 5-, 9- and 12-year-olds, respectively). Although the programme was initiated in 2001, not all schools were included initially due to logistic reasons and the supplementation programme was phased over a period of time. The interval between megadose supplementation in children ranges from 9 months (between first and second dose) to 3 years (between fourth and final dose) (Family Health Bureau, 2000).

Vitamin A intervention programmes require rigorous and repeated evaluation to ensure they are achieving their goal (Wasantwisut, 2002). The national vitamin A supplementation programme in Sri Lanka has not been evaluated for its efficacy at any level since its inception. We report here an evaluation of the programme in school children in a selected area of Sri Lanka.

Abbreviations: DDHS, Divisional Director of Health Services; MOH, Medical Officer of Health.

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Materials and methods

Study site and subjects

A cross-sectional study was carried out in the Yatiyantota Medical Officer of Health (MOH)/Divisional Director of Health Services (DDHS) area in the Kegalle District of the Sabaragamuwa Province from May to August 2002. Sri Lanka has nine provinces and each province is divided into districts and each district is divided into a number of MOH/DDHS areas administered by a MOH/DDHS. Each MOH/DDHS area has a population ranging from 70 000 to 100 000. The country is thus divided into 270 MOH/DDHS areas. In a survey carried out in 1995–6, the Sabaragamuwa province had the highest percentage of children with low serum retinol concentrations (less than 0·7 μmol/l) (Medical Research Institute, 1998). Approximately half of the school children in the area were supplemented with the vitamin A oral megadose (105 μmol) at the time of the survey. Each dose contained 105 μmol vitamin A and 9·1mg vitamin E. Capsules were manufactured by Accucaps Industries Ltd (Windsor, Canada). As supplementation was carried out in Grades 1 and 4, the survey was carried out among children in Grades 1, 2, 4 and 5. A sample of ninety-five children was required from each category to estimate a prevalence of night blindness of 1 % with a 95 % CI ranging from 0 to 3 %.

There were seventy-six schools in the area. The list of schools of the Yatiyantota DDHS area and their supplementation status were obtained from the DDHS. Supplemented children were recruited from seven randomly selected schools in which the supplementation programme was carried out. Non-supplemented children were recruited from two randomly selected schools in which the supplementation was not carried out.

Evaluation of ocular manifestations of vitamin A deficiency

Night blindness was assessed by history and by examining children in a dimly lit room at least 12 feet in length with several items of furniture (World Health Organization, 1996). Mothers and children were questioned about night blindness with appropriate terms in the local language to obtain a history of night blindness. All children were subject to a clinical examination to detect ocular manifestations of vitamin A deficiency by trained medical officers according to the guidelines specified by the World Health Organization (1995*a*).

Socio-demographic and anthropometric data

An interviewer-administered questionnaire was used to collect information on socio-demographic and health-related data. Anthropometric measurements were obtained according to WHO guidelines (World Health Organization, 1995*b*). The height of each child was measured to a precision of 0·1 cm using a measuring scale. Weights were measured to a precision of 0·1 kg using a digital electronic scale (Seca, Les Mureaux, France). The scale was standardised every twenty-fifth to thirtieth measurement with standard weights of 500 g and 5 and 10 kg. Previous heights and weights of the children were obtained from past school medical inspection records. Anthropometric indices were calculated using EPIINFO (Centers for Disease Control and Prevention, Atlanta, GA, USA) and children were classified as stunted, underweight or wasted if their *z*-score of height-for-age, weight-for-age or weight-for-height was less than two standard deviations below the National Center for Health Statistics median. *z*-scores for weight-for-height were calculated for males up to 138 months (11.5 years) of age and less than 145 cm and for females up to 120 months (10 years) of age and less than 137 cm.

Collection of morbidity data

Morbidity data were collected by questioning the mothers on the past history of diarrhoea and respiratory infections in children during the 4 weeks prior to the interview. Diarrhoea was defined as the passage of three or more loose motions a day and a respiratory infection was defined as the presence of cough with or without expectoration for at least 24 h.

Determination of serum vitamin A concentrations

A 2 ml sample of venous blood was drawn from each child and transferred at 4°C to a laboratory in Colombo within 4–5 h where serum was separated and stored at −80°C until biochemical analysis. Serum vitamin A concentrations were assayed by reversed-phase HPLC according to the method of Bieri *et al.* (1979). A total of 200 μl serum was added to 100 μl standard solution of retinyl acetate and 100 μl ethanol and serum vitamin A was extracted with 600 μl hexane. A 400 μl portion of the hexane extract was evaporated to dryness under a stream of nitrogen gas, re-dissolved in 100 μl mobile phase, and injected on to a C_{18}, reversed phase 150 mm × 4·6 mm HPLC column (5 μm particle size; Waters, MA, USA). The mobile phase (methanol–water, 95:5 v/v) was delivered at a flow rate of 1 ml/min. Vitamin A (eluting time 4 min) was detected at 325 nm in a Beakman ultraviolet detector. The vitamin A concentration was quantified to the peak area of the internal retinyl acetate standard. The CV was 7·2 % and inter-batch CV was 5·8 %. Serum vitamin A values are reported in μmol/l.

Statistical analyses

Data analyses were carried out using SPSS (SPSS Inc., Chicago, IL, USA). *t* Tests, χ^2 tests and regression analysis were used to detect associations.

Ethical aspects

Ethical clearance to conduct the study was obtained from the Ethical Review Committee of the Faculty of Medical Sciences, University of Sri Jayewardenepura. Permission to conduct the study was obtained from the Deputy Provincial Director of Health Services, Kegalle District, the Zonal Director of Education, Dehiowita, and all principals of schools selected for the study. Children were recruited into the study after obtaining written informed consent from their parents or guardians. Children detected with signs of vitamin A deficiency were given an oral megadose of vitamin A. Children with other medical conditions were referred appropriately.

Results

A total of 746 students from nine schools in the Yatiyantota MOH/DDHS area were recruited into the study. A total of 452 children from seven schools were supplemented with vitamin A. The rest (*n* 294) were not supplemented. The socio-demographic profile of the children is given in Table 1.

The majority of the non-supplemented children were female, older than 9 years and lived in permanent houses. Mothers of supplemented children were more educated than mothers of non-supplemented children.

The prevalence of eye signs and symptoms among school children was extremely low and there was no difference between supplemented and non-supplemented children (Table 2). When the analyses were performed considering the sexes separately, there was no significant difference in nutritional status between supplemented and non-supplemented boys. Girls supplemented with vitamin A tended to be more malnourished than their non-supplemented counterparts (data not shown). Among non-supplemented children, only one case of night blindness was detected by history. Among supplemented children, five children had night blindness by dark adaptometry.

Although the nutritional status of supplemented children was poorer than that of the non-supplemented children, only the difference for height-for-age was statistically significant (Table 2). There was no significant difference in the reported incidence of infections between the two groups of children.

Of the supplemented children who were stunted at the last school medical examination 53 % were normal in the current survey (Table 3). Among the non-supplemented children classified as stunted in the last school medical examination, 23 % were classified as normal in the current survey.

Serum vitamin A concentrations of supplemented children (1·4 (SD 0·49) μmol/l) were significantly higher than those of controls (1·2 (SD 0·52) μmol/l) ($P=0{\cdot}003$). Serum vitamin A concentrations declined gradually from the time of supplementation (Table 4; Fig. 1). Serum vitamin A concentrations of the children who were supplemented more than 6 months prior to the survey (1·3 (SD 0·44) μmol/l in those supplemented 7–12 months back and 1·1 (SD 0·44) μmol/l in those supplemented 13–18 months back) were similar to those of control children (1·2 (SD 0·52) μmol/l). Children who were supplemented within 1 month had the highest serum vitamin A concentrations (1·6 (SD 0·45) μmol/l) followed by children supplemented 1–6 months (1·4 (SD 0·50) μmol/l) previously.

In a multiple regression analysis, taking serum vitamin A concentrations as the dependent variable, time since supplementation (<1 month, 1–6 months, 7–12 months and >12 months) was the only significant predictor of serum vitamin A concentrations after controlling for other variables

Table 1. Socio-demographic profile of children

	Supplemented		Non-supplemented			
Variable	*n*	%	*n*	%	χ^2	*P* value
Sex						
Male	237	52·4	110	37·4	16·15	<0·001
Female	215	47·6	184	62·6		
Total	452	100·0	294	100·0		
Age (years)						
<7	177	39·3	54	21·5	42·40	<0·001
7–9	109	24·2	42	16·7		
>9	164	36·4	155	61·8		
Total	450	100·0	294	100·0		
Mother's education						
Up to primary	82	19·2	46	18·0	6·76	0·034
Secondary	147	34·4	113	44·1		
≥ GCE OL/AL	198	46·4	97	37·9		
Total	427	100·0	256	100·0		
Father's education						
Up to primary	89	21·2	41	16·8	3·89	0·143
Secondary	157	37·4	109	44·7		
≥ GCE OL/AL	174	41·4	94	38·5		
Total	420	100·0	244	100·0		
Father's occupation						
Unskilled worker/labourers	198	46·2	106	39·6	3·82	0·431
Skilled workers	130	30·3	84	31·3		
Professional	29	6·8	24	9·0		
Business	57	13·3	42	15·7		
Not with the family/died	15	3·5	12	4·5		
Total	429	100·0	268	100·0		
Number of family members						
<5	224	49·8	132	46·1	0·92	0·337
≥5	226	50·2	154	63·9		
Total	450	100·0	286	100·0		
Type of house						
Temporary/semi-permanent	121	27·0	45	15·6	12·43	<0·001
Permanent	328	73·0	242	84·4		
Total	449	100·0	287	100·0		

GCE OL/AL, GCE ‘O’ level/‘A’ level.

Table 2. Health profile of children

Variable	Supplemented *n*	Supplemented %	Non-supplemented *n*	Non-supplemented %	χ^2	*P* value
Ocular manifestations						
Bitot's spots						
Present	6	1·3	1	0·3		0·257*
Absent	445	98·7	283	99·7		
Conjunctival xerosis						
Present	9	2·0	6	2·1		1·000*
Absent	442	98·0	278	97·9		
Night blindness by evaluation of dark adaptation						
Present	5	1·1	0	0·0		0·163*
Absent	446	98·9	284	100·0		
Night blindness by history						
Present	5	1·1	1	0·3		0·414*
Absent	446	98·9	283	99·7		
Anthropometric status†						
Weight-for-age						
Underweight	144	32·1	65	26·3	2·571	0·109
Normal	304	67·9	182	73·7		
Total	448	100·0	247	100·0		
Weight-for-height						
Wasting	80	19·5	34	16·7	0·663	0·416
Normal	331	80·5	169	83·3		
Total	411	100·0	203	100·0		
Height-for-age						
Stunting	81	18·8	28	11·3	6·514	0·011
Normal	351	81·3	220	88·7		
Total	432	100·0	248	100·0		
Reported diseases 4 weeks prior to the survey						
Diarrhoea						
Experienced	43	9·5	23	7·8	3·07	0·381
Not experienced	409	90·5	271	92·2		
Cough and cold						
Experienced	302	66·8	181	61·6	2·15	0·142
Not experienced	150	33·2	113	38·4		

* Fisher's Exact Test.
† Children were classified as stunted, underweight or wasted if their *z*-score of height-for-age, weight-for-age or weight-for-height was less than two standard deviations below the National Center for Health Statistics median.

(Table 5). Children who were supplemented within 6 months of the survey had a higher serum vitamin A concentration than controls. The difference was as much as 0·4 μmol/l within 1 month of the survey and 0·2 μmol/l between 1 and 6 months.

Discussion

The present study clearly shows that children supplemented with vitamin A within 1 month had a significantly higher concentration of vitamin A than those supplemented earlier. The ability

Table 3. Prevalence of stunting* in the last school medical examination and current survey in relation to vitamin A supplementation status

Vitamin A supplementation status	Current survey: Stunted *n*	Stunted %	Normal *n*	Normal %	Total *n*	Total %
Supplemented						
Last school medical examination						
Stunted	55	46·6	63	53·4	118	100·0
Normal	15	06·0	235	94·0	250	100·0
McNemar's test: $\chi^2 = 28{\cdot}3$; $P<0{\cdot}001$						
Non-supplemented						
Last school medical examination						
Stunted	10	76·9	3	23·1	13	100·0
Normal	4	02·6	150	97·4	154	100·0
McNemar's test: $\chi^2 = 0{\cdot}0$; $P=1{\cdot}000$						

* Children were classified as stunted if their *z*-score of height-for-age was less than two standard deviations below the National Center for Health Statistics median.

Table 4. Serum vitamin A concentrations and prevalence of vitamin A deficiency by duration since supplementation*

	Serum vitamin A concentrations (μmol/l)			Prevalence of vitamin A deficiency†	
Duration since supplementation	*n*	Mean	SD	*n*	%
<1 month	97	1·6[a]	0·45	3	3·1
1–6 months	126	1·4[b]	0·50	10	7·9
7–12 months	46	1·3[c]	0·44	6	13·0
13–18 months	79	1·1[c]	0·44	17	21·5
Controls	162	1·2[c]	0·52	30	18·5
F/χ^2 value		2·747‡		20·784§	
P value		<0·001		<0·001	

[a,b,c] Mean values within a column with unlike superscript letters were significantly different ($P<0·05$; Student–Newman–Keuls test).
* For details of procedures, see p. 154.
† For vitamin A deficiency, a serum vitamin A concentration of 0·7 μmol/l was taken as the cut-off value.
‡ *F* test from ANOVA.
§ χ^2 value.

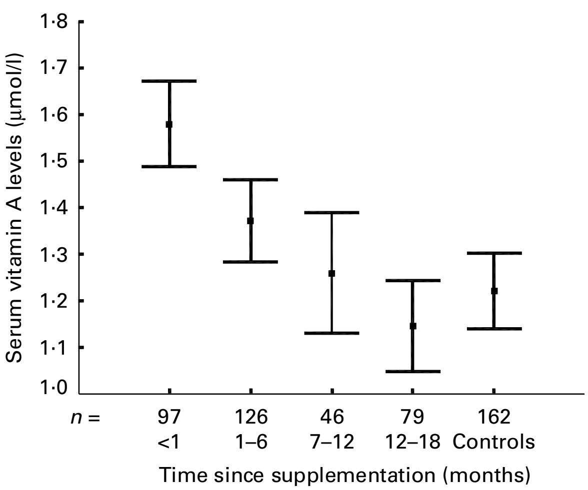

Fig. 1. Serum vitamin A levels by time since supplementation. For details of procedures, see p. 154. Values are means with their 95 % CI depicted by vertical bars.

to sustain a high serum vitamin A concentration following an oral megadose depends on many factors. The higher demand for nutrients during the period of growth, inadequate consumption of vitamin A and increased catabolism of vitamin A under a heavy burden of parasitic infections are critical to the vitamin A status of a child (Semba, 1994). Some children were living on estates where a high prevalence of geo-helminth infections had been reported (Sorensen *et al.* 1996; Gunawardena *et al.* 2005). Supplemented children came from a poorer socioeconomic background and this may be a reason for their inability to sustain a high serum vitamin A level after 6 months of supplementation.

The single most important predictor of vitamin A levels was the time since supplementation, with vitamin A levels declining over time. Immediately after supplementation, vitamin A levels may increase by as much as 0·4 μmol/l, i.e. a 30–40 % increase in serum levels. By the end of 6 months this drops by about 0·2 μmol/l.

The dose of 105 μmol (100 000 IU) used in the supplementation programme in Sri Lanka may be a reason for the rapid decline in vitamin A levels. Different dosage and frequency forms have been used elsewhere. Most studies using a megadose of 210 μmol (200 000 IU) for supplementation every 3–4 or 6 months report beneficial effects despite co-existing malnutrition and heavy infectious disease burdens (Sommer *et al.* 1986; West *et al.* 1991; Daulaire *et al.* 1992). In Africa, the Ghana Vast Study Team (1993) trial reported the beneficial effects of vitamin A supplementation on morbidity and mortality on children over 1 year with children receiving 210 μmol every 4 months. Herera *et al.* (1992) reported that a 6-monthly dosing schedule of vitamin A supplementation had no impact on child survival in Sudan. Similarly, Pedro *et al.* (2004) reported that the effect of high-dose vitamin A capsules on serum retinol concentrations do not persist for 6 months in children from 1 to 5 years of age in the Philippines.

The success of a vitamin A supplementation programme using an oral megadose relies on the body's ability to store vitamin A. The bulk of the body's vitamin A is stored as retinyl esters in the liver. To meet constant tissue needs, despite day-to-day variability of dietary vitamin A, a steady concentration of circulating retinol is maintained by drawing on hepatic reserves through secretion of retinol bound to its specific carrier protein, retinol-binding protein (Gamble *et al.* 2001). Protein deficiency status reduces the absorption of vitamin A, and the synthesis and release of retinol-binding protein from the liver. In such situations, an oral megadose supplementation programme will be ineffective.

Donnen *et al.* (1998) reported that high-dose supplementation of vitamin A did not reduce morbidity in malnourished and vitamin A-deficient children, and recommended a daily low-dose vitamin A supplementation for severely malnourished children. There is evidence that weekly low-dose supplementation is more effective than periodic megadose supplementation (Rahmathullah *et al.* 1990). More frequent supplementation schedules have inherent practical problems associated with their implementation.

Baseline vitamin A status may influence the impact of a supplementation programme. It has been reported that serum concentrations will only increase if they are already low and low concentrations are due to vitamin A deficiency (Olson, 1984). We could not elucidate baseline values as the survey was a cross-sectional survey. Considering average vitamin A concentrations of children which ranged from 1·4 (SD 0·49)

Table 5. Regression analysis using serum vitamin A levels (μmol/l) as the dependent variable

Independent variable	β*	df	SE	*F*/*t* value	*P* value
Intercept	1·315	1			
Supplementation†		4		7·407‡	<0·001
< 1 month	0·348	1	0·071	4·918§	<0·001
1 − 6 months	0·173	1	0·065	2·665§	0·008
7 − 12 months	0·082	1	0·089	0·951§	0·342
12 − 18 months	− 0·014	1	0·079	− 0·177§	0·859
Sex‖	− 0·093	1	0·049	− 1·902§	0·058
Mothers' educational status¶		2		1·042‡	0·353
Up to primary	− 0·102	1	0·078	− 1·307§	0·192
Secondary	− 0·006	1	0·057	− 0·104§	0·917
Father's educational status**		2		0·280‡	0·756
Up to primary	− 0·034	1	0·073	− 0·470§	0·639
Secondary	0·014	1	0·058	0·242§	0·809
Type of house††	− 0·028	1	0·055	− 0·502§	0·616
Age (months)‡‡	− 0·001	1	0·001	− 0·363‡	0·716

* Regression coefficient.
† Reference group is the control group.
‡ *F* test.
§ *t* test.
‖ Reference group is female children.
¶ Reference group is education above Grade 9.
** Reference group is education above Grade 9.
†† Reference group is permanent house type.
‡‡ Reference group is children ≥5 years.

to 1·2 (SD 0·52) μmol/l for supplemented and control groups, respectively, there is very little evidence to suggest a high prevalence of vitamin A deficiency or extreme deficiency among these children. The average serum vitamin A concentrations in children of the present study were similar to those reported in the UK (Thurnham *et al.* 2005) and USA (Ballew *et al.* 2001), though measured using different assays. It is possible that the impact of a single mega dose supplementation of 105 μmol vitamin A observed in the present study may be due to the relatively low prevalence of vitamin A deficiency in this population.

Serum vitamin A levels and the prevalence of ocular manifestations of deficiency are important outcome indicators in evaluating vitamin A intervention programmes (Wasantwisut, 2002). Though vitamin A concentrations were significantly different between non-supplemented and supplemented children 6 months before the survey, there was no significant difference in the prevalence of ocular manifestations of vitamin A deficiency or morbidity between the two groups of children. It may be concluded that a single dose of 105 μmol vitamin A improved serum vitamin A concentrations significantly in the short term but the effect on morbidity was not clear.

Night blindness and conjunctival xerosis are often associated with poor nutritional status, particularly stunting (Brink *et al.* 1979; Santos *et al.* 1983). There are reports that vitamin A supplementation improves linear growth (Arroyave *et al.* 1979; Muhilal *et al.* 1988; Hadi *et al.* 2000). Even though the single administration of a 105 μmol megadose may be inadequate to sustain high levels after 6 months, there is evidence suggestive that it may have a beneficial effect on nutritional status of children as documented by the reduction in the prevalence of stunting in supplemented children. However, the present results need to be interpreted with caution given the baseline differences, and age and sex differences between the two groups.

A typical child in a developing country would need to increase the portion size of fruits and vegetables by about 10-fold to control vitamin A deficiency by eating fruits and vegetables alone, a goal which cannot be achieved (Miller *et al.* 2002). Therefore, without supplementation, a child in a developing country is not able to attain and maintain 'minimally adequate' vitamin A stores in the liver. The WHO recommends a dose of 210 μmol vitamin A every 4–6 months for children above 1 year of age (World Health Organization, 2000). Hence, the dose of 105 μmol every 3 years used in Sri Lanka for school children is grossly inadequate.

The problem of overdosing may be the single most important reason for using the current dosing schedule. Only about 1 % of children showed signs of intolerance to 210 μmol retinyl palmitate in acid solution, which disappeared after a few hours (Arroyave, 1988). Sommer (1996) did not report any deaths linked to isolated vitamin A toxicity. Studies conducted among preschool children receiving 210 μmol every 4–6 months reported no overdosing signs and symptoms (Sommer *et al.* 1986; West *et al.* 1991; Daulaire *et al.* 1992).

In Sri Lanka, vitamin A deficiency has been a long-felt public health problem and there was no sustained programme prior to the current supplementation programme. Although supplementation with high-dose vitamin A is the most widely used strategy to combat vitamin A deficiency, other strategies have been adopted or are being considered in other countries. These include food fortification, homestead food production and social marketing (Bloem *et al.* 2002). Revising the dosing schedule coupled with other interventions may produce better results.

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