# Serum retinol in 1–6-year-old children from a low socio-economic South African community with a high intake of liver: implications for blanket vitamin A supplementation

Martha E van Stuijvenberg<sup>1,\*</sup>, Serina E Schoeman<sup>1</sup>, Carl J Lombard<sup>2</sup> and Muhammad A Dhansay<sup>1,3</sup>

<sup>1</sup>Nutritional Intervention Research Unit, Medical Research Council, PO Box 19070, Tygerberg 7505, Cape Town, South Africa: <sup>2</sup>Biostatistics Unit, Medical Research Council, Cape Town, South Africa: <sup>3</sup>Executive Directorate Research, Medical Research Council, Cape Town, South Africa

Submitted 13 February 2011: Accepted 8 July 2011: First published online 23 August 2011

# **Abstract**

*Objective:* To assess serum retinol, liver intake patterns, breast-feeding history and anthropometric status in pre-school children of a low socio-economic community where liver is regularly consumed.

Design: Cross-sectional study.

Setting: Northern Cape Province, South Africa.

Subjects: Children aged 1–6 years (n 243) who attended the local primary health-care facility and had not received a vitamin A supplement in the 6 months preceding the study. Non-pregnant female caregivers (n 225), below 50 years of age, were also assessed.

Results: Despite stunting, underweight and wasting being prevalent in 40.5%, 23.1% and 8.4% of the children, only 5.8% had serum retinol concentrations  $<20\,\mu\mathrm{g}/\mathrm{dl}$ , which is in sharp contrast to the national prevalence of 63.6%. None of the caregivers were vitamin A deficient. Liver was eaten by 89.2% of children, with 87% of households eating liver at least once monthly and 30% eating it at least once weekly; liver was introduced into the diet of the children at a median age of 18 months. Ninety-three per cent of the children were being breast-fed or had been breast-fed in the past; children were breast-fed to a median age of 18 months. A significant negative correlation was found between educational level of the caregiver and frequency of liver intake (r = -0.143, P = 0.032). There was no correlation between serum retinol and indicators of anthropometric or socio-economic status.

*Conclusions:* The blanket approach in applying the national vitamin A supplementation programme may not be appropriate for all areas in the country, even though the community may be poor and undernourished.

Keywords Serum retinol Liver intake Pre-school children Vitamin A supplementation

Vitamin A deficiency continues to be a public health problem in many developing countries and is estimated to affect 190 million pre-school children globally<sup>(1)</sup>. The primary cause of vitamin A deficiency is insufficient intake of animal products containing preformed vitamin A or plant foods containing β-carotene. Supplementing children between 6 months and 5 years of age with vitamin A has been shown to reduce all-cause mortality by 23–34%<sup>(2-4)</sup>. As a result, periodic high-dose vitamin A supplementation has been recommended in countries where more than 15% of the under-5 population have serum retinol concentrations below 20 μg/dl<sup>(5)</sup>, or where the under-5 mortality rate exceeds 70 deaths per 1000 live births<sup>(6)</sup>. In South Africa, a national high-dose vitamin A supplementation programme, targeting 6–59-month-old

children at public health facilities, as well as postpartum women within 6–8 weeks after delivery, was introduced in 2002<sup>(7)</sup>.

While vitamin A supplementation undoubtedly has benefits and has been shown to save lives in severely vitamin-A-deficient children<sup>(8)</sup>, there are indications that high-dose vitamin A supplementation may increase morbidity in children who are not deficient in vitamin A, especially with regard to lower respiratory tract infections<sup>(9)</sup>. Concerns regarding the universal application of vitamin A supplementation have been expressed by several authors in the past<sup>(10–12)</sup>, and more recently in a comprehensive commentary by Latham<sup>(13)</sup>, in which he challenges the wisdom and validity of regularly providing massive doses of vitamin A to children, especially those

who are not vitamin A deficient. Latham argues that vitamin A capsules were originally intended as a short-term emergency measure for areas where severe vitamin A deficiency is present, that it is not sustainable, and that it may act as a policy barrier impeding more sustainable food-based approaches. He further maintains that vitamin A programmes do not reach the 10–20% in greatest need and moreover that there is no certainty that vitamin A programmes are not doing harm in populations where vitamin A status is sufficient<sup>(13)</sup>.

In South Africa, according to a recent survey, the national prevalence of vitamin A deficiency (serum retinol  $<20 \,\mu\text{g/dl}$ ) in 1–9-year-old children is  $63.6 \,\%^{(14)}$ . However, South Africa is a country that is diverse in terms of culture, geography and socio-economic status, and this diversity is also reflected in the eating habits of its population. Vitamin A deficiency, for example, varies between provinces, with the prevalence being the highest in KwaZulu-Natal (88.9%) and the lowest in the Northern Cape  $(23.0\%)^{(14)}$ . There may also be pockets where, due to unique eating patterns, vitamin A deficiency may not be present at all. Baseline data from an Fe fortification trial in 6-9-year-old schoolchildren from a Northern Cape community during 2002 showed that vitamin A deficiency, contrary to expectation, was virtually absent despite high levels of poverty, stunting and underweight<sup>(15)</sup>. These children were not exposed to vitamin A supplementation during their pre-school years and further investigation revealed a regular intake of liver (15), which is a concentrated source<sup>(16)</sup> of preformed vitamin A.

The prevalence of vitamin A deficiency in the under-5 s from this community, i.e. the age group targeted by the vitamin A supplementation programme, is not known. The aim of the present study was to assess serum retinol, liver intake patterns, breast-feeding history and anthropometric status in the pre-school children of this 'liver eating' community, and to also obtain information on the vitamin A status of the caregiver.

# Methods

### Study population and design

The study was undertaken in Calvinia-West. This is the low socio-economic section of the town of Calvinia, which is situated in the Hantam district of the Northern Cape Province and approximately 470 km north of Cape Town. The area is characterised by arid conditions, and plant foods are not cultivated or frequently consumed in the area. Sheep farming is the main industry. The Northern Cape Province is the largest of the nine South African provinces, but the smallest in terms of population size, and has the highest levels of stunting and underweight in the country<sup>(14)</sup>.

The study was a cross-sectional one of the pre-school children and their female caregivers attending the primary health-care facility in Calvinia-West during the period April to November 2008. Because national data showed the prevalence of vitamin A deficiency in the 7-9-year-old age group to be also above  $60\%^{(14)}$ , all pre-school children visiting the health facility, irrespective of age, were included in the study. Assuming a vitamin A deficiency prevalence of 5%, and specifying the precision level of a two-sided 95% CI as 3%, a sample size of 203 was required, using the 'Large Sample Normal Approximation'. For inclusion in the study, the child should have been accompanied by the caregiver who was responsible for the child's food, and should not have received a vitamin A supplement in the 6 months that preceded the assessment date (i.e. was due for his/her next vitamin A supplement according to national supplementation protocol, whereby children aged 6-11 months should receive a single dose of 100 000 IU (30 000 µg retinol equivalents, RE) and children aged 12-59 months receive a dose of 200 000 IU (60 000 μg RE) every 6 months). The term 'caregiver' includes the child's biological mother and is used as such throughout the text. If a child presented with a fever he/she was not recruited for the study. Only nonpregnant caregivers below 50 years of age were included for anthropometric and biochemical measurements. If a caregiver visited the health facility with more than one child, the other children were also included in the study, but the caregiver's anthropometric and vitamin A status was not assessed again. Door-to-door visits, as well as the local radio station, were used to inform mothers and caregivers about the project, and to encourage them to bring their children to the health facility. This resulted in those who do not regularly attend the facility also being surveyed. A nationwide vitamin A supplementation campaign took place during September 2008 but, at the request of the researchers, was postponed in the Calvinia area until after completion of our study.

The study was approved by the Ethics Committee of the South African Medical Research Council, and permission was obtained from both the provincial and national Departments of Health. Written informed consent was obtained from the caregiver of each participant.

# Measurements

## Biochemical indicators

Blood (5 ml) from the caregiver and child was obtained via antecubital venepuncture, before the child received a vitamin A supplement as per protocol. Blood was centrifuged at the site, using a portable centrifuge, and serum removed and stored at  $-20^{\circ}$ C until collected by a member of the research team who visited the study site at regular intervals. Care was taken throughout the process to protect blood samples from direct sunlight. At the Medical Research Council in Cape Town, samples were stored at  $-80^{\circ}$ C until analysed. Serum retinol was determined, under dimmed light, by a reversed-phase HPLC method which is based on the method described by Catignani and Bieri<sup>(17)</sup>.

The CV (intra- and inter-assay) for this method is <4%. Serum C-reactive protein (CRP) was measured as an indicator of infection by means of an ELISA method (DRG Diagnostics, Marburg, Germany).

## Anthropometric indicators

Weight was measured in light clothing and without shoes to the nearest 0.05 kg using an electronic load cell scale (UC-321 Personal Precision Health Scale; A&D Company, Ltd., Tokyo, Japan). The accuracy of the scale was checked against a standard weight at regular intervals. Recumbent length of children younger than 2 years was measured to the nearest 0·1 cm on a horizontally placed measuring board with a fixed headboard and a moveable foot-piece. Height of the caregivers and children aged ≥ 2 years was measured to the nearest 0.1 cm using a wooden board with a fitted measuring tape and a moveable head-piece. Measurements were taken by trained fieldworkers whose measurements and technique were validated against that of a researcher. Height and weight were expressed as height-for-age, weightfor-age and weight-for-height Z-scores using the WHO growth standards<sup>(18)</sup>. Date of birth and birth weight were obtained from the child's Road to Health card (RTHC).

#### *Questionnaire information*

A questionnaire, administered through an interview with the caregiver, was used to obtain information on socioeconomic status, liver intake and breast-feeding history. History of vitamin A supplementation (dosage and date) was obtained from the child's RTHC.

# Statistical analysis

Data were checked for normal distribution by using the Kolmogorov–Smirnov test for normality and analysed using the PASW (formerly SPSS) statistical software package version 18·0 (SPSS Inc., Chicago, IL, USA). Continuous data were expressed as mean (standard deviation or 95% confidence interval) or when not normally distributed as median (interquartile range). Categorical data were reported as percentages. Spearman's correlation coefficients were used to test for correlations between continuous variables. *P* values below 0·05 were considered statistically significant.

# Results

The study comprised 243 pre-school children and 225 caregivers. The characteristics and socio-economic status of the study population is given in Table 1. The majority (89·3%) of the caregivers were the biological mother of the child. The age of the children ranged between 1 and 6 years, with the majority being between 2 and 4 years old. Approximately half of the caregivers were single, i.e. had never been married nor lived with a partner. Only 15% completed high school, while 33% had 7 years or less of schooling. About 72% were unemployed, and

about 37% were dependent on a relative or social grant as their main source of income.

The anthropometric status of the children and caregivers is shown in Table 2. The prevalence of stunting, underweight and wasting was approximately double the national prevalence and, according to WHO criteria, can be classified as 'very high', 'high' and 'medium to high', respectively. Birth weight was below 2500 g in 28·1% of the children. Only  $12\cdot2\%$  of caregivers were underweight (BMI <  $18\cdot5$  kg/m²), but  $28\cdot8\%$  were stunted using the WHO height-forage reference median for 18-year-old girls and assuming the caregiver's height had not changed since.

None of the children were exposed to vitamin A supplementation in the 6 months before the study, and almost 40% had never received a vitamin A supplement; 77% received no supplements in the past 18 months (Table 3). There was no correlation between supplementation history (months since last supplement) and serum retinol levels of the child. The serum retinol status of the children and their caregivers is shown in Table 4 and Fig. 1. Mean serum retinol in the children was 31.3 µg/dl, and only 5.8% were vitamin A deficient (serum retinol < 20 µg/dl), which is considerably lower than the national prevalence of 63.6%. None of the children had serum retinol concentrations < 10 µg/dl. In the caregivers, mean serum retinol was 55·1 µg/dl, which is double the national mean. None had serum retinol concentrations < 20 µg/dl, while 9% (nineteen individuals) presented with serum retinol concentrations in excess of 75 µg/dl, and two individuals with levels above 100 µg/dl. There was a significant positive correlation between the serum retinol concentration of the caregiver and that of the child (r = 0.156; P = 0.023). CRP concentrations were raised in 6.4% of the children and in 16.3% of the caregivers, which was similar to the national figures (Table 4). Morbidity data, retrospectively collected during the survey, showed diarrhoea to have occurred in 2.9% and acute respiratory infections in 16.0% of the children during the 4 weeks that preceded the study. A significant negative correlation between CRP and serum retinol levels in both the child and the caregiver was found (r = -0.225; P = 0.001 and r = -0.181; P = 0.011, respectively). When CRP concentrations  $\geq 10 \,\mathrm{mg/l}$  were excluded from the data set, the prevalence of vitamin A deficiency in the children was 4.9%. There was no significant correlation between serum retinol levels and the age or anthropometric status of the child, or any of the measured indicators of socio-economic status.

The liver-eating patterns of the study population are shown in Table 5 and Fig. 2. Liver was eaten in almost all households (98·2%), while almost 90% of the pre-school children reportedly ate liver; 57% of households ate liver during the 2 weeks that preceded the study. Liver was introduced into the diet of the child at a median age of 18 months, and 45% had been eating liver from the age of 12 months or younger. The majority of households (87%) ate

**Table 1** Characteristics and socio-economic status of the study population: children and their female caregivers visiting a primary health-care facility in a low socio-economic area in the Northern Cape Province, South Africa, April–November 2008

	n	Mean or %	SD	Range
Children (n 243)				
Age (years)	243	3.53	1.30	1.2-6.3
Age distribution (%)				
1·0–1·9 years	31	12.8		
2·0–2·9 years	66	27.2		
3·0–3·9 years	57	23.5		
4·0–4·9 years	42	17.3		
5·0-5·9 years	43	17.7		
6·0–6·5 years	4	1.6		
Gender (male; %)	119	49.0		
Caregivers (n 243)				
Biological mother	217	89.3		
Guardian/relative	26	10∙7		
Age (years)	210	29.90	7.45	16.5–47.6
Age distribution (%)				
<20 years	16	7.6		
20·0–29·9 years	92	43.8		
30·0–39·9 years	76	36.2		
≥ 40 years	26	12.4		
Socio-economic indicators				
Marital status (n 225)				
Married	62	27.6		
Living together	53	23.6		
Widow/divorced/separated	7	3⋅1		
Single (never married/not living with partner)	103	45.8		
Educational level (n 225)				
Grade 0–3	17	7.6		
Grade 4–7	58	25.8		
Grade 8–11	116	51⋅6		
Grade 12	33	14.7		
Tertiary education	1	0.4		
Employment status (n 225)				
Currently employed	64	28.4		
Currently unemployed	161	71.6		
Main source of income (n 225)				
Own income	36	16∙0		
Spouse/partner	86	38.2		
Combined income (own + partner)	20	8.9		
Parent/other relative	40	17⋅8		
Social grant	43	19.1		

liver at least once monthly while as many as 30% reported eating liver at least once weekly (Fig. 2). There was a significant negative correlation between educational level of the caregiver and the frequency of liver intake in the household  $(r=-0.143;\ P=0.032)$ , but no correlation between the frequency of liver intake and serum retinol in either the mother or the child. Ninety-three per cent of the children were either being breast-fed at the time of the study or had been breast-fed in the past. Children were breast-fed to a median age of 18 months (Table 6). The liver-eating patterns of the breast-feeding mothers did not differ from those of the mothers not breast-feeding at the time of the study.

# Discussion

Vitamin A deficiency is usually associated with low socio-economic conditions and poor anthropometric status<sup>(1,14,19,20)</sup>. However, in the present study, despite high

levels of poverty, stunting and underweight, subclinical vitamin A deficiency was prevalent in only 5.8% of the pre-school population. No correlation was found between serum retinol and socio-economic or anthropometric status. The virtual absence of vitamin A deficiency in this Northern Cape community is in sharp contrast to the national prevalence of  $63.6\%^{(14)}$ , and likely to be due to a regular consumption of liver by both the mother and the child, as well as a breast-feeding prevalence of more than 90%.

Sheep farming is the main industry in the area and abattoir activities take place on a daily basis. Owing to this there is a regular surplus of organ meat, which is not exported to other parts of the country, resulting in liver being available in this community at low cost (<\$US 0.5/kg liver) and often distributed via informal trading. The inverse relationship between educational level and frequency of liver consumption suggests that it is the poorer people, i.e. those most vulnerable to vitamin A deficiency, who consume liver most. It would thus appear as if this

Table 2 Anthropometric status of children and their female caregivers visiting a primary health-care facility in a low socio-economic area in the Northern Cape Province, South Africa, April–November 2008

	Study population		SA national data*	
	Mean or prevalence	95 % CI	Mean or prevalence	95 % CI
Children				
Stunted (%)+	40.5	34.2, 46.8	18.0	16.4, 19.6
Underweight (%)‡	23·1	17.8, 28.5	9.3	8.1, 10.5
Wasted (%)§	8.4	4.5, 12.3	4.5	3.6, 5.4
Mean birth weight (g; n 235)	2753	2678, 2828		
Birth weight < 2500 g (%)	28·1	22.3, 33.8		
Caregivers (n 205)				
Mean BMl (kg/m²)	25.5	24.6, 26.5	26.5	26.2, 26.7
BMI distribution (%)		•		,
<18·5 kg/m <sup>2</sup>	12.2	7.7, 16.7	4.6	3.7, 5.4
18·5–24·9 kg/m²	39.5	32.8, 46.2	43.9	42.0, 46.0
25·0–29·9 kg/m <sup>2</sup>	26.3	20.3, 32.4	26.6	25.2, 28.8
≥ 30·0 kg/m <sup>2</sup>	22.0	16.3, 27.6	24.9	23.3, 26.7
Mean height (cm)	153-5	152.5, 154.4		,
Stunted (%)	28.8	22.6, 35.0		

<sup>\*</sup>South African national food consumption survey[14].

**Table 3** History of vitamin A supplementation according to the clinic card (*n* 243) among children visiting a primary health-care facility in a low socio-economic area in the Northern Cape Province, South Africa, April–November 2008

	n	% of children
Number of months since last vitamin A supplement		_
≤6.0	0	0
6·1–12·0	28	11∙5
12·1–18·0	28	11∙5
18·1–24·0	21	8.6
24·1–30·0	27	11.1
30·1–36·0	16	6.6
>36.0	27	11.1
Never	96	39.5
Total number of vitamin A supplements received		
No supplements	96	39.5
1 supplement	103	42.4
2 supplements	43	17·7
3 supplements	1	0.4
Number of vitamin A supplements received during the 18 months preceding the stud	ly	
No supplements	187	77.0
1 supplement	50	20.6
2 supplements	6	2.5

impoverished community has an inherent 'survival mechanism' that protects them against vitamin A deficiency. This regular consumption of liver by the poor is in contrast to elsewhere in Africa where cost was shown to be a major factor limiting liver consumption<sup>(21)</sup>. The lack of correlation between frequency of liver intake and serum retinol concentrations is probably a reflection of the adequate vitamin A status of this population; serum retinol is known to be homeostatically controlled and reflects body stores only when the latter are very low or very high<sup>(19)</sup>.

In the South African national survey<sup>(14)</sup>, children were included for vitamin A measurements irrespective of

whether they received a high-dose vitamin A supplement during the previous 6 months or not. One of the strengths of our study is that children who received a vitamin A supplement during the preceding 6 months, according to their health card records, were not included in the study. The adequate vitamin A status in this population is therefore unlikely to be attributed to the vitamin A supplementation programme. This is further supported by the fact that 77% of the children had not received a vitamin A supplement during the last 18 months, and that as many as 40% had never been exposed to vitamin A supplementation in the past.

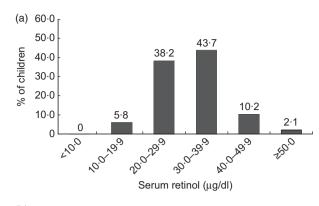
tHeight-for-age (*n* 232), ‡weight-for-age (*n* 242) and \$weight-for-height (*n* 191) *Z*-scores <-2 sp of the WHO reference median; the National Center for Health Statistics reference standards were used in the national survey and, when applied to our study population, the prevalence of stunting, underweight and wasting was 33·6%, 26·0% and 10·3%, respectively.

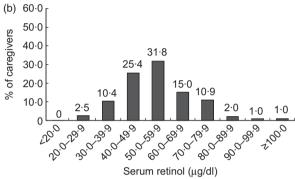
||Height-for-age *Z*-score <-2 sp of the WHO reference median for girls aged 18 years.

Table 4 Serum retinol concentrations of children and their female caregivers visiting a primary health-care facility in a low socio-economic area in the Northern Cape Province, South Africa April–November 2008

		Study po	Study population			SA national data*	al data*	
	Children ( <i>n</i> 243)	43)	Caregivers (n 202)	202)	Children aged 1-9 years (n 1397)	ars (n 1397)	Women (n 1847)	147)
	Mean or prevalence	95 % CI	Mean or prevalence	95 % CI	Mean or prevalence 95 % Cl Mean or prevalence 95 % Cl Mean or prevalence	95% CI	Mean or prevalence 95% CI	95% CI
Serum retinol concentration (μg/dl)†‡	31.28	31.3, 32.3	55.10	53.1, 57.1	17.8	17.3, 18.4		26.5, 28.3
Proportion with serum retinol below 20 µg/dl (%)	2.8	2.9, 8.7	0	I	63.6	61.0, 66.1	27.2	25.2, 29.2
Proportion with CRP concentration ≥ 10 mg/l (%)\$	6.4	3.1, 9.6	16.3	11.2, 21.5	6.9	5.6, 8.3		10.6, 13.5

South African national food consumption survey<sup>[14]</sup>. 1  $\mu$ g/dl = 0.035  $\mu$ mol/l. Mean and 95 % Cl. Prevalence and 95 % Cl. Prevalence and 95 % Cl. Prevalence and 95 % Cl. For CRP, n 220 (children); n 196 (caregivers); n 1429 (SA children); n 1939 (SA women).



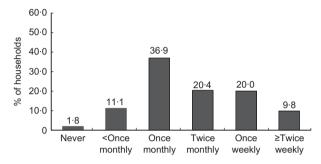


**Fig. 1** (a) Distribution of serum retinol in pre-school children visiting a primary health-care facility in a low socio-economic area in the Northern Cape Province of South Africa, April–November 2008 (*n* 243). None of these children received a vitamin A supplement in the preceding 6 months and were therefore eligible for vitamin A supplementation according to national vitamin A supplementation guidelines; blood was taken before the child received the vitamin A capsule. (b) Distribution of serum retinol in female caregivers of the preschool children visiting the primary health-care facility (*n* 202)

Liver is an excellent, but often underappreciated, source of preformed vitamin A, with sheep liver containing approximately 7800 µg retinol activity equivalents (RAE)/100 g<sup>(16)</sup>. The estimated average daily requirement (EAR) for children aged 1-3 and 4-8 years is 210 and 275 µg RAE, respectively 222. This translates into a liver intake of only 3.5 g/d (or the equivalent of only 98 g liver/ month) necessary to meet the vitamin A requirement of a 4-8-year-old child. We did not quantify liver intake but, based on previous unpublished observations, as well as preliminary data from a current study quantifying dietary intake in this population, an average portion size of 60 g in this age group was assumed. A 4-8-year-old child who consumes liver twice monthly would thus have 121% (334 µg RAE) of his/her daily vitamin A needs met by the liver intake alone. Those who consume liver once weekly would have 243% (669 µg RAE) of their vitamin A needs met, while those who consume liver twice weekly or more would have a vitamin A intake of at least 1337 µg RAE/d, i.e. 4.9 times the EAR and exceeding the upper intake level (UL) of 900 µg RAE by 48%. These estimates do not take into account the contribution of other foods containing vitamin A, such as bread or maize meal, which 722 ME van Stuijvenberg *et al.* 

Table 5 Liver-eating patterns in the study population: children and their female caregivers visiting a primary health-care facility in a low socio-economic area in the Northern Cape Province, South Africa, April–November 2008

	n	Proportion (%)	95 % CI
Households in which liver is eaten ( <i>n</i> 225)	221	98·2	96.5, 99.9
Households that ate liver during the last 2 weeks (n 225)	128	56-9	50.4, 63.4
Children who eat liver (n 240)	214	89-2	85.2, 93.1
Age liver introduced into diet (n 212)			•
Children eating liver from the age of ≤ 24 months (%)	166	78.3	72.8, 83.9
Children eating liver from the age of ≤ 12 months (%)	95	44.8	38.1, 51.5
Age at which liver was introduced into diet of child (months)			*
Median		18.0	
Interquartile range		12.0–24.0	



**Fig. 2** Distribution of the frequency of liver consumption at household level among pre-school children and their female caregivers visiting a primary health-care facility in a low socioeconomic area in the Northern Cape Province of South Africa, April–November 2008 (*n* 225)

are fortified with vitamin A and several other micronutrients, according to the national food fortification regulations<sup>(23)</sup>. Bread is a staple food in this community, and assuming a consumption of 4 slices daily, an additional 80–90 µg RAE would be provided by bread.

Liver is also a good source of other micronutrients such as Fe, Zn and B-vitamins<sup>(16)</sup>. However, in relation to its vitamin A content, liver contains considerably less of these micronutrients, and to meet the EAR for Fe and Zn, for example, liver would have to be consumed on a daily basis. Besides this not being feasible, liver, if eaten every day, may lead to an overload of vitamin A, as seen in case reports where liver, eaten several times a week for extended periods, resulted in severe cases of toxicity in young children<sup>(24,25)</sup> and adults<sup>(26)</sup>.

The food-based approach is being advocated as the preferred way to prevent and control micronutrient deficiencies<sup>(27)</sup>. In the study community, liver is a favourite food, especially among poorer people, and a sustainable food-based vitamin A 'intervention' is therefore already in place. A concern in this low socio-economic Northern Cape community, however, is the high levels of stunting and underweight compared with the rest of South Africa. While vitamin A requirements are being met by the intake of liver, the children from this community are likely to suffer deprivation of various other nutrients, including Ca. There are, for example, indications of limited intakes of

milk (other than breast milk), fresh fruit and vegetables in this population (J Nel, unpublished results). Providing children with regular high-dose vitamin A capsules – which they do not need – may lull health authorities into a false sense of security, believing that the children's nutritional needs are being attended to and that no further intervention is required. It also raises concerns of vitamin A excess in those sections of the population that eat liver at least once weekly and, in addition, regularly receive vitamin A capsules.

High-dose vitamin A supplementation is not without risk. Apart from the transient effects such as headache, nausea, vomiting, fever, diarrhoea and bulging of the anterior fontanel<sup>(28)</sup>, there are indications that vitamin A supplementation may increase respiratory tract infections in vitamin-A-sufficient children<sup>(9)</sup>. It is hypothesised that pharmacological doses of vitamin A given to children with adequate vitamin A stores may cause temporary dysregulation of the immune system, leading to increased susceptibility to infections (12). In mice, excessive intake of vitamin A has been shown to increase the risk and severity of asthma by exacerbating allergic airway inflammation and pulmonary hyper-responsiveness<sup>(29)</sup>. Accidental overdosing during vitamin A campaigns is also a risk, as was seen in India where thirty deaths were reported in children receiving higher than the recommended dosage during a nationwide campaign<sup>(30)</sup>. Recently there has been growing concern regarding the chronic effects of subclinical vitamin A toxicity. In adults, a long-term intake of preformed vitamin A of only twice the RDA has been associated with osteoporosis and hip fractures, presumably by stimulating bone resorption and inhibiting the ability of vitamin D to prevent Ca loss from the bone (31–33). The long-term effect of periodic high-dose vitamin A supplements on the bone health of young children is not known, especially those who are vitamin A sufficient but compromised in terms of other micronutrients.

A limitation of the present study is that it does not include data from children below 1 year of age. It was, however, difficult to obtain blood from this age group. This is unfortunate, because younger children usually have a greater vulnerability to infections and vitamin A deficiency. However, the adequate vitamin A status of the

**Table 6** Current or past breast-feeding practices in the study population: children and their female caregivers visiting a primary health-care facility in a low socio-economic area in the Northern Cape Province, South Africa, April–November 2008

	n	Proportion of children (%)	95 % CI
Breast-feeding practice	239		
Currently breast-fed	60	25⋅1	19.6, 30.6
Previously breast-fed	162	67⋅8	61.9, 73.7
Never breast-fed	17	7⋅1	3.9, 10.4
Duration of breast-feeding (months)	161		
<2	14	8.7	4.4, 13.1
2–3	20	12.4	7.3, 17.5
4–6	16	9.9	5.3, 14.6
7–12	19	11.8	6.8, 16.8
13–18	12	7.4	3.4, 11.5
19–24	43	26.7	19.9, 33.5
>24	37	23.0	16.5, 29.5
Age breast-feeding stopped (months)			,
Median		18∙0	
Interquartile range		5.0-24.0	

mothers, and the fact that children are being breast-fed for extended periods, makes severe vitamin A deficiency in the under-1 children from this community unlikely.

#### Conclusions

The virtual absence of vitamin A deficiency in the study community highlights the fact that, although national data from a country indicate a public health problem, there may be pockets within that country that are different due to unique eating habits and local circumstances. Although the results of the present study pertain to only a small section of the South African population, there are indications that people from surrounding areas, where sheep farming is a major activity, have similar levels of liver consumption. An extensive survey is currently underway to establish how many of these 'liver eating' pockets exist in the country and where. Our results have important implications for the national vitamin A supplementation programme, in that the blanket approach in applying the programme may not be appropriate for all areas in the country, even though the community may be poor and undernourished.

## Acknowledgements

Sources of funding: This work was supported by the Medical Research Council, Cape Town, South Africa, as well as by a grant from SIGHT AND LIFE, Basel, Switzerland. Conflict of interest: The authors have no conflict of interest. Authors' contributions: M.E.v.S. and S.E.S. conceptualised and designed the study, collected and analysed the data, and wrote the manuscript; C.J.L. was responsible for the statistical aspects of the study; M.A.D. contributed to the conceptualisation and design of the study, and writing of the manuscript. Acknowledgements: The authors thank the mothers and children who participated in the study; the staff of the Calvinia-West primary

health-care facility; J. Nel, D. Sass, A. van Jaarsveld, S. van Zyl, M. Cloete, Y. Hannah and F. Venter who assisted with the fieldwork; E. Harmse and M. Marais who analysed the blood samples; and the Department of Health for giving permission to conduct the study.

#### References

- World Health Organization (2009) Global Prevalence of Vitamin A Deficiency in Populations at Risk 1995–2005. WHO Global Database on Vitamin A Deficiency. Geneva: WHO
- 2. Beaton GH, Martorell R, Aronson KJ et al. (1993) Effectiveness of Vitamin A Supplementation in the Control of Young Child Morbidity and Mortality in Developing Countries. Nutrition Policy Discussion Paper no. 13. Toronto: Canadian International Development Agency.
- Fawzi WW, Chalmers TC, Herrera G et al. (1993) Vitamin A supplementation and child mortality. A meta-analysis. IAMA 269, 898–903.
- Glasziou PP & Mackerras DEM (1993) Vitamin A supplementation in infectious diseases: a meta-analysis. *BMJ* 306, 366–370.
- Sommer A & Davidson FR (2002) Assessment and control of vitamin A deficiency: the Annecy Accords. *J Nutr* 132, 9 Suppl., S2845–S2850.
- UNICEF (2007) Vitamin A Supplementation. A Decade of Progress. New York: UNICEF.
- Department of Health (2004) Guidelines for the Implementation of Vitamin A Supplementation. Pretoria: Nutrition Directorate, Department of Health.
- West KP Jr, Klemm RDW & Sommer A (2010) Vitamin A saves lives. Sound science, sound policy. World Nutr 1, 211–229.
- Chen H, Zhuo Q, Yuan W et al. (2008) Vitamin A for preventing acute lower respiratory tract infections in children up to seven years of age. Cochrane Database Syst Rev. issue 1, CD006090.
- Dhansay MA (2003) Vitamin A supplementation: a case of not seeing the wood for the trees? S Afr J Clin Nutr 16, 116–117.
- 11. Fawzi WW (2006) The benefits and concerns related to vitamin A supplementation. *J Infect Dis* **193**, 756–759.
- 12. Grotto I, Mimouni M, Gdalevich M et al. (2003) Vitamin A supplementation and childhood morbidity from diarrhea

- and respiratory infections: a meta-analysis. *J Pediatr* **142**, 297–304.
- 13. Latham M (2010) The great vitamin A fiasco. World Nutr 1, 12–45.
- Labadarios D (editor) (2007) National Food Consumption Survey: Fortification Baseline South Africa, 2005. Pretoria: Department of Health.
- Van Stuijvenberg ME, Smuts CM, Wolmarans P et al. (2006)
   The efficacy of ferrous bisglycinate and electrolytic iron as fortificants in bread in iron-deficient school children. Br J Nutr 95, 532–538.
- Wolmarans P, Danster N, Dalton A et al. (editors) (2010) Condensed Food Composition Tables for South Africa. Cape Town: Medical Research Council.
- 17. Catignani GL & Bieri JG (1983) Simultaneous determination of retinol and α-tocopherol in serum or plasma by liquid chromatography. *Clin Chem* **29**, 708–712.
- World Health Organization (2006) Child Growth Standards. Length/Height-for-Age, Weight-for-Age, Weight-for-Length, Weight-for-Height and Body Mass Index for age. Methods and Development. Geneva: WHO.
- World Health Organization (1996) Indicators for Assessing Vitamin A Deficiency and Their Application in Monitoring and Evaluating Intervention Programmes. Geneva: WHO.
- Ahmed F, Azim A & Akhtaruzzaman M (2003) Vitamin A deficiency in poor, urban, lactating women in Bangladesh: factors influencing vitamin A status. *Public Health Nutr* 6, 447–452.
- 21. Nana CP, Brouwer ID, Zagré NM *et al.* (2006) Impact of promotion of mango and liver as sources of vitamin A for young children: a pilot study in Burkina Faso. *Public Health Nutr* **9**, 808–813.
- Food and Nutrition Board, Institute of Medicine (2001) Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese,

- Molybdenum, Nickel, Silicon, Vanadium, and Zinc. Washington, DC: National Academy Press.
- Department of Health (2003) Regulations relating to the fortification of certain foodstuffs. http://www.doh.gov.za/ docs/regulations/2003/ffortification.html (accessed January 2011).
- 24. Carpenter TO, Pettifor JM, Russel RM *et al.* (1987) Severe hypervitaminosis A in siblings: evidence of variable tolerance to retinol intake. *J Pediatr* **111**, 507–512.
- Mahoney PC, Margolis MT, Knauss TA et al. (1980) Chronic vitamin A intoxication in infants fed chicken liver. Pedriatrics 65, 893–897.
- Selhorst JB, Waybright EA, Jennings S et al. (1984) Liver lover's headache: pseudotumor cerebri and vitamin A intoxication. JAMA 252, 3365.
- Thompson B & Amoroso L (editors) (2011) Combating Micronutrient Deficiencies: Food-Based Approaches. Rome: FAO and CABI.
- Sommer A & West KP Jr (editors) (1996) Supplementation. In Vitamin A Deficiency. Health, Survival, and Vision, pp. 388–409. New York: Oxford University Press.
- Schuster GU, Kenyon NJ & Stephensen CB (2008) Vitamin A deficiency decreases and high dietary vitamin A increases disease severity in the mouse model of asthma. *J Immunol* 180, 1834–1842.
- 30. Kapil U (2004) Update on vitamin A-related deaths in Assam, India. *Am J Clin Nutr* **80**, 1082–1083.
- Penniston KL & Tanumihardjo SA (2006) The acute and chronic toxic effects of vitamin A. Am J Clin Nutr 83, 191–201.
- Promislow JHE, Goodman-Gruen D, Slymen DJ et al. (2002) Retinol intake and bone mineral density in the elderly: the Rancho Bernardo study. J Bone Miner Res 17, 1349–1358.
- 33. Michaëlsson K, Lithell H, Vessby B *et al.* (2003) Serum retinol levels and risk of fracture. *N Engl J Med* **348**, 287–294.