

## High prevalence of vitamin A deficiency is detected by the modified relative dose-response test in six-month-old Senegalese breast-fed infants. Agne-Djigo

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### Introduction

Newborns have very low stores of vitamin A at birth, regardless of their mother's vitamin A status during pregnancy, so infants depend on adequate vitamin A intake from breast milk, other vitamin A-rich foods, or vitamin A supplements (VAS) to build their hepatic vitamin A reserves post-partum. Breast milk vitamin A concentration reflects maternal vitamin A status, dietary vitamin A intake, and (during the first half of infancy) maternal receipt of early post-partum VAS. Researchers in Senegal have recently examined the vitamin A status of six-month-old infants to assess their vitamin A status in relation to whether or not their mothers reported receiving VAS after delivery. These observations form the basis of this month's NNA review.

### Methods

The investigators recruited infants ~6 months of age and their mothers during routine immunization sessions at urban health centers in Dakar. The primary purposes of the study were to establish baseline maternal plasma and breast milk retinol concentrations prior to the initiation of a national program to fortify vegetable oil with vitamin A, and to compare subsequently the responsiveness of the two indicators of population vitamin A status. At the same time, infant milk intake was measured by using the deuterium-to-mother tracer method, and infant vitamin A status was assessed by measuring plasma retinol concentration and completing a modified relative dose response test (MRDR). Infant vitamin A status markers were compared for those whose mothers reported that they did or did not receive high-dose VAS during the early post-partum period.

### Results and conclusions

From a total of 59 mother-infant pairs enrolled in the study, 25 mothers refused to allow infant blood sampling, so results are available for 34 mother-infant pairs. The overall mean plasma retinol concentration of the mothers was 1.7  $\mu\text{mol/L}$ , and the mean breast milk vitamin A concentration was 1.5  $\mu\text{mol/L}$ . These results did not differ significantly for mothers who reportedly did or did not receive early post-partum VAS. However, three of 19 reportedly non-supplemented mothers had plasma retinol concentrations between 0.70 and 1.05  $\mu\text{mol/L}$ , whereas none of the 13 mothers who stated that they had received VAS post-partum had values in this marginal range ( $p=0.13$ ).

All of the infants were still breast feeding, although most were also receiving other foods. Infants of supplemented mothers consumed an average of 0.9 L breast milk/d, and infants of non-supplemented mothers consumed an average of 0.8 L breast milk/d ( $p=0.06$ ). Mean vitamin A intake from breast milk did not differ significantly for the two groups (1.4 versus 1.6  $\mu\text{mol/L}$ , respectively;  $p=0.52$ ). The mean plasma retinol concentration of infants of supplemented mothers did not differ significantly from those of infants of non-supplemented mothers (0.9  $\mu\text{mol/L}$  versus 0.8  $\mu\text{mol/L}$ , respectively;  $p=0.32$ ). On the other hand, the mean MRDR ratio among infants of non-supplemented

mothers was significantly greater (i.e., more likely to indicate low hepatic vitamin A reserves) than the mean MRDR ratio among infants of supplemented mothers ( $0.074 \pm 0.017$  versus  $0.056 \pm 0.017$ , respectively, after adjusting for infant age;  $p=0.015$ ). A total of 95% of the infants of non-supplemented mothers had low hepatic reserves according to the MRDR test, compared with 54% of the infants of supplemented mothers ( $p=0.006$ ). The investigators concluded that the majority of these infants had evidence of low hepatic vitamin A reserves at ~six months of age, and infants whose mothers stated that they did not receive VAS post-partum were more likely to be deficient.

### **Program and Policy Implications**

These results suggest that VAS of infants at six months of age may be necessary to ensure that they have adequate hepatic reserves and to protect them against future vitamin A deficiency, especially when breast milk is being replaced by complementary foods with low vitamin A content. The World Health Organization currently recommends that infants and young children 6-59 months of age in areas where vitamin A deficiency is considered to be a public health problem should receive periodic, high dose VAS (WHO, 2011). Evidence indicates that VAS reduces all-cause mortality among these children (Mayo-Wilson, 2011). VAS are being delivered during semi-annual child health days in many African countries (Aguayo, 2007), but this strategy fails to reach a large proportion of infants at exactly six months. Thus, novel approaches to schedule VAS at six months need to be developed, possibly by linking VAS with a new child contact point at six months for immunizations and counseling on complementary feeding.

WHO does not currently recommend VAS for early post-partum women, newborns, or infants 1-5 months of age to prevent maternal and infant morbidity and mortality (WHO, 2011). However, the WHO guidelines affirm that maternal post-partum supplementation may increase breast milk vitamin A concentration and infant vitamin A status. Studies are currently under way to provide additional information on the impact of newborn VAS on infant mortality and morbidity.

### **NNA Editors' comments\***

The results of the present study suggest that low hepatic vitamin A reserves may be a common problem among 6-month-old Senegalese infants, but several limitations of the study must be recognized. Firstly, the research was conducted in a convenience sample of infants attending immunization clinics in Dakar, so it is not possible to extrapolate this information to the national population. Secondly, the mothers self-reported whether or not they received VAS post-partum, and the results could not be verified. Moreover, because the women were not randomly assigned to supplementation groups, the vitamin A-related outcomes could be confounded by possible selection biases. Finally, it is somewhat puzzling that the women apparently had adequate vitamin A status and breast milk vitamin A contents, yet the infants were found to be deficient, even though they were consuming adequate amounts of vitamin A from breast milk. This set of findings calls into question whether the cutoff applied for the MRDR results is appropriate for this age group, particularly because reference data are not available from presumably well nourished infants.

Despite the uncertainties in interpretation of these results, the findings highlight the potential usefulness of programs designed to deliver VAS to infants at exactly six months of age. The study further emphasizes the need to evaluate existing vitamin A assessment methods for their applicability during infancy and to develop related reference data for this age period.

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\* These comments have been added by the editorial team and are not part of the cited publication.

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