



IVACG Statement

Safe Doses of Vitamin A

During Pregnancy and Lactation

Vitamin A is needed in increased amounts to support maternal reproductive processes, including fetal growth and development, and during lactation to replace losses in breast milk. The increased need during gestation is small and can be provided through a balanced diet and maternal reserves from well-nourished women.¹ In areas of endemic vitamin A deficiency (VAD), however, vitamin A supplements often must supply this need. With lactation, requirements rise to replace maternal vitamin A lost daily in breast milk and to maintain breast milk vitamin A at a level to protect the needs of rapidly growing infants during at least the first 6 months of life.²

Vitamin A requirements to support repetitive reproductive cycles may be difficult to meet from the affordable vegetarian-type diets typical of VAD areas,³ but they are easily provided through a high-dose or frequent low-dose vitamin A supplement. High doses of vitamin A given in early pregnancy can be unsafe, and it is operationally difficult to provide daily small doses in developing countries. Intervention programs to meet vitamin A needs of fertile women, therefore, must adjust dose levels and timing to ensure safety during pregnancy and lactation.

Severe VAD in animals causes abortions, fetal death, resorptions, and congenital defects.⁴ These outcomes occur in rats when maternal tissue is depleted to the extent that reserves are decreased in the ocular system, one of the last tissues to lose its vitamin A supply.⁵ Case reports of adverse reproductive outcomes associated with human deficiency are rare and poorly documented. Available epidemiologic observations in human populations where clinical vitamin A deficiency in children is common also rarely report adverse reproductive outcomes. This is in spite of

recognizing that reproductive-age women living in VAD areas frequently report night blindness during pregnancy and/or lactation⁶ and that nightblindness in women during periods of increased physiologic need is thought to reflect vitamin A deficiency. However, an association of incident congenital ocular defects with

VAD is suggested by a recent randomized community trial in pregnant Nepalese women. Ocular defects were reduced in their newborns by weekly low-dose vitamin A supplementation.⁷

High doses of vitamin A—retinol, retinyl ester, and their oxidized metabolites—given to animals in the

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early gestational period can cause congenital defects,⁸ and reports suggest impaired growth and behavioral response rates when high doses are given later in gestation.^{9,10} Dose and timing when adverse effects are noted are highly variable and species specific.

In humans, malformations similar to those seen in animals have been recorded when women ingested high doses of preformed vitamin A and related compounds (particularly retinoic acid and analogues) in the first trimester.¹¹

Retinoic acid and other oxidized metabolites are not used in VAD control programs and, in fertile women, only under medical supervision for specialized conditions when they are not pregnant. Birth defects from ingestion of retinol or retinyl ester, usually occur when the high-dose supplement is taken daily for several days or weeks during the first gestational trimester.⁸ There is no evidence of acute toxicity from ingesting β -carotene or other carotenoids from supplements or food, especially at levels comparable to those recommended for vitamin A supplementation.^{11,12}

Night blindness is frequently reported in pregnant women living in areas where VAD is common in children,¹³ and breast milk from lactating women residing in these areas is often low in vitamin A.¹⁴ Night blindness during pregnancy has sometimes been reported to disappear without intervention following parturition, but may reappear during lactation and/or repeat pregnancies.^{6,13} Night blindness associated with pregnancy and lactation is reported to be only partially responsive to vitamin A supplementation,^{4,6,15} which suggests that other nutritional deficiencies may contribute to the problem.

Breast milk levels of vitamin A in a population reflect habitual maternal vitamin A intakes, particularly when low. Low vitamin A levels have been safely increased in populations, including lactating women, when the ingestion of vitamin A–fortified food products becomes frequent^{16,17} and in individual mothers provided low-dose vitamin A supplements daily (2000 IU)¹⁸ or up to 300,000 IU in a single dose given within 1 month of parturition.¹⁹ Fully breast-feeding mothers are

infertile for at least 8 weeks postpartum²⁰ and, while amenorrheic, are of low susceptibility to pregnancy up to 6 months.²¹ The physiologic needs for vitamin A of infants born to vitamin A–adequate mothers and fed breast milk with adequate vitamin A (in excess of 30 $\mu\text{g}/\text{dL}$ or 1.05 $\mu\text{mol}/\text{L}$) are met for at least the first 6 months of life.²

The World Health Organization recently convened a group of experts to consider dose and safety issues in relationship to the vitamin A needs of fertile women and their nursing infants.²⁰ The consultation responded in part to a single report questioning the safety

of daily intakes during pregnancy of 10,000 IU vitamin A as a supplement given to adequately nourished women in the United States.²² Recently available global population-based information was also reviewed on the length of postpartum infertility, the period when it would be safe to give high doses of vitamin A to reproductive-age women. The review of both published and available unpublished data reconfirmed earlier recommendations of IVACG (1986) that:

- It is safe to give fertile women, independent of their vitamin A status, as much as 10,000 IU (3000 μg RE) daily at any time during pregnancy.

There is no evidence of acute toxicity from ingesting β -carotene or other carotenoids from supplements or food, especially at levels comparable to those recommended for vitamin A supplementation.

The recommendation was extended by noting that:

- No benefits have been demonstrated from taking a supplement during gestation where habitual vitamin A intakes exceed about three times the RDA (about 8000 IU or 2400 µg RE) from sources rich in provitamin A.

The earlier recommendations of IVACG for supplementation of women residing in endemically deficient areas also were extended to include the following timing and doses:

- A weekly supplement of up to 25,000 IU (8500 µg RE) is a safe alternative to daily supplementation during pregnancy.*

- A single high-dose supplement of up to 200,000 IU to breast-feeding women is safe up to 8 weeks postdelivery.
- For non-breast-feeding women, a single high-dose supplement of up to 200,000 IU is safe up to 6 weeks postdelivery.

Fortified food products can safely be ingested during pregnancy and lactation, and vitamin A-rich natural foods, such as animal liver, consumed occasionally also can be safely ingested.^{20,23} There is no known teratogenic risk associated with prolonged consumption of either natural food sources or supplements rich in vitamin A–active carotenoids.^{8,12}

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*During the first 60 days following conception, the advisability of doses above 25,000 IU is uncertain. Risks are likely to diminish as gestation advances.

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Established in 1975, the International Vitamin A Consultative Group guides international activities for reducing vitamin A deficiency in the world. IVACG concentrates its efforts on stimulating and disseminating new knowledge, translating that new knowledge to assist others in its practical application, and providing authoritative policy statements and recommendations that others can use to develop appropriate prevention and control programs.

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