Proceedings of the XX International Vitamin A Consultative Group Meeting

Extent of Vitamin A Deficiency among Preschool Children and Women of Reproductive Age[1,2]

Keith P. West, Jr.[3]

Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD 21205

ABSTRACT Knowledge of the extent of vitamin A (VA) deficiency (D) is critical for identifying high-risk populations and mobilizing resources for prevention. Yet, all estimates are necessarily imperfect, often based on assumptions in the absence of data. In 1995, the World Health Organization estimated 254 million children to be VA-deficient and 2.8 million to have xerophthalmia. Subsequently, estimates were changed to 75–140 million and 3.3 million, respectively. Although both sets are consistent with a problem of enormous magnitude, the discrepancies also created uncertainty. The present analysis indicates there are ~127 million and 4.4 million preschool children with VAD (serum retinol < 0.70 μmol/L or displaying abnormal impression cytology) and xerophthalmia, respectively. More than 7.2 million pregnant women in the developing world are VA-deficient (serum or breast-milk vitamin A concentrations < 0.70 μmol/L), and another 13.5 million have low VA status (0.70–1.05 μmol/L); >6 million women develop night blindness (XN) during pregnancy annually. Roughly 45% of VA-deficient and xerophthalmic children and pregnant women with low-to-deficient VA status live in South and Southeast Asia. These regions harbor >60% of all cases of maternal XN, three fourths of whom seem to live in India. Africa accounts for 25–35% of the global cases of child and maternal VAD; about 10% of all deficient persons live in the eastern Mediterranean region, 5–15% live in the Western Pacific and ~5% live in the Region of the Americas. VA prophylaxis seems to be preventing the number of deficient preschool children from increasing while probably reducing rates of blindness and mortality. Greater effort is needed to assess and prevent VAD and its disorders, particularly among pregnant and lactating women. J. Nutr. 132: 2857S–2866S, 2002.

KEY WORDS: • *vitamin A deficiency* • *night blindness* • *xerophthalmia* • *prevalence* • *global-burden of disease*

Vitamin A deficiency (VAD)[4] is a major public health nutrition problem in the developing world. It especially affects young children, among whom deficiency can cause xerophthalmia and lead to blindness, limit growth, weaken innate and acquired host defenses, exacerbate infection and increase the risk of death (1). It is also becoming clear that VAD can extend through school age and adolescent years into adulthood. Although the health consequences of VAD are not well delineated beyond early childhood, recent data indicate that VAD in women of reproductive age may increase morbidity and mortality during pregnancy and the early postpartum period (2–4). Severe maternal VAD may also disadvantage the newborn, leading to increased mortality in the first months of life (5–7). As consequences of VAD (now collectively known as vitamin A deficiency disorders; VADD) (**Fig. 1**) (8,9) become increasingly recognized, it is crucial that the resultant health burden be quantified as precisely as possible, as a basis for action and subsequent monitoring and evaluation of preventive programs.

Considerable progress has been made over the past 4 decades in estimating the burden of VAD, principally by aggregating and extrapolating prevalence data from countries where it has been collected in populations with a similar demographic profile and anticipated risk. In recent years, VAD has been estimated to affect between 75 (10) and 254 (11) million preschool children each year, a far from precise range. No

[1] Presented at the XX International Vitamin A Consultative Group (IVACG) Meeting, "25 Years of Progress in Controlling Vitamin A Deficiency: Looking to the Future," held 12–15 February 2001 in Hanoi, Vietnam. This meeting was co-hosted by IVACG and the Local Organizing Committee of the Vietnamese Ministry of Health and representatives of United Nations technical agencies, the private sector, multilateral agencies and nongovernmental organizations in Vietnam, with funding from the government of Vietnam. The Office of Health, Infectious Disease and Nutrition, Bureau for Global Health, U.S. Agency for International Development, assumed major responsibility for organizing the meeting. Conference proceedings are published as a supplement to the *Journal of Nutrition*. Guest editors for the supplement publications were Alfred Sommer, Johns Hopkins University, Baltimore, MD; Frances R. Davidson, U.S. Agency for International Development, Washington; Usha Ramakrishnan, Emory University, Atlanta, GA; and Ian Darnton-Hill, Columbia University, New York, NY.

[2] Preparation of this paper was supported by Cooperative Agreement HRN-A-00-97-00015-00 between the Office of Health and Nutrition; U.S. Agency for International Development (Washington); and the Center for Human Nutrition, Department of International Health, The Bloomberg School of Public Health, Johns Hopkins University (Baltimore, Maryland), with additional support from The Bill and Melinda Gates Foundation (Seattle, Washington) and the Task Force Sight and Life Research Institute.

[3] To whom correspondence should be addressed. E-mail: kwest@jhsph.edu.

[4] Abbreviations used: CIC, conjunctival impression cytology; DHS, Demographic Health Surveys; FSM, Federated States of Micronesia; IVACG, International Vitamin A Consultative Group; MDIS, Micronutrient Deficiency Information System; SD, standard deviation; VAD, vitamin A deficiency; VADD, VAD disorders; WHO, World Health Organization; XN, night blindness.

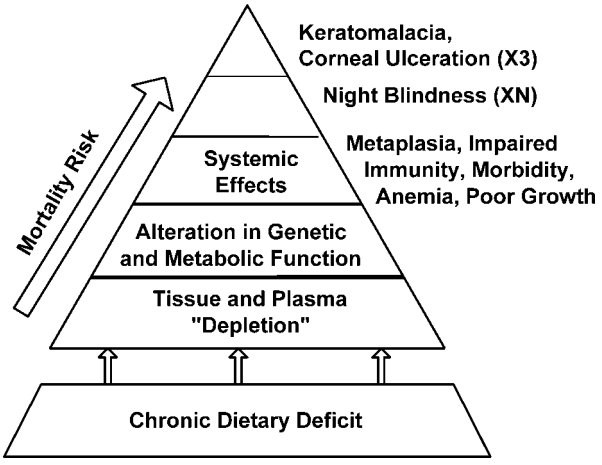

FIGURE 1 Spectrum of vitamin A deficiency disorders (VADD).

estimates of the global burden of maternal VAD or the annual incidence of maternal night blindness (XN) exist. This article updates existing information on the numbers of preschool-aged children with VAD and xerophthalmia and provides a first approximation of the numbers of pregnant women likely to be vitamin A deficient and night blind each year.

METHODS

Sources of data

An extensive array of data relevant to the extent of VAD was reviewed, including the comprehensive, annotated assembly of survey results on VAD compiled by the Micronutrient Deficiency Information System (MDIS) of the World Health Organization (WHO) in 1995 (11), augmented by a preliminary MDIS update in the year 2001 (12); an in-depth analysis and report on population burden and trends in VAD in preschool-aged children conducted by Sethuraman and colleagues in 1998 (10), hereafter referred to as the MI report, which incorporated previous MDIS estimates of VAD with country updates from 107 UNICEF program offices and other sources; published surveys and field studies in which vitamin A status of children or women are reported; and unpublished reports, meeting presentations and personal communications about recent surveys not included in previous analyses. This last set of "gray literature" sources consisted of abstracts of presentations at meetings of the International Vitamin A Consultative Group (IVACG) and survey summaries in specialized publications, bulletins and newsletters from ministries of health, multilateral and bilateral agencies and nongovernmental organizations. Where possible, sources were contacted for further information on survey data not readily available in the public domain.

The main demographic groups at risk of VADD and of interest for this analysis are preschool-aged children (i.e., <5 y of age) and pregnant women. Data on vitamin A status reported for more narrow preschool ages (e.g., 6–36 mo) or for preschool age groups that also included children beyond the fifth year of life were taken to represent preschooler status. Where data permitted, findings on the vitamin A status of women were restricted to pregnancy. However, because of the sparsity of population-based vitamin A status data on pregnant women, clinical and biochemical findings obtained in surveys and field studies of nonpregnant women of reproductive age, especially during the first 6 mo postpartum, were assumed to reflect the status of pregnant women and thus were used for this initial estimation.

Population estimates of the number of preschool-aged children in each country, against which prevalence rates were applied to estimate the absolute numbers affected, were obtained from the UNICEF Year 2001 State of the World's Children Report, with 1999 serving as the reference year (13). The number of pregnant women each year was conservatively derived from the annual number of live births reported for each at-risk country by UNICEF for the year 1999 (13), without adjustment for miscarriages and stillbirths.

Indicators of VAD

Biochemical and cytologic indicators. Serum (or plasma) retinol distributions provided the primary data for assessing the extent of VAD in children and women (1). For countries that lacked serological data, the frequency of abnormal conjunctival impression cytology (CIC)[5] or the distribution of vitamin A concentration in breast milk, both considered for the purpose of this analysis to be roughly comparable with serum retinol for estimating population prevalence (14–20), were used where available to estimate the extent of VAD in children and women, respectively. A serum or plasma retinol concentration < 0.70 μmol/L was taken to represent deficiency in children (21). Among women, two retinol concentration cutoffs were used to estimate VAD and low to deficient vitamin A status, respectively (16,17): <0.70 and <1.05 μmol/L. Prevalence rates below cutoffs were accepted as reported by the investigators. However, when serological or breast-milk retinol data were given only as a mean and SD or standard error of the mean (with numbers of subjects), prevalences were derived by assuming data were normally distributed and calculating standard normal deviates (z-scores) and probabilities associated with areas under the left tail of the normal curve. Surveys in which both mean (SD) and actual cutoff data were reported provided a basis for evaluating the validity of the normalized estimate. For example, in Ecuador the mean (SD) of serum retinol in preschool children was 0.97 (0.32) μmol/L (22). Under assumptions of "normality," the standardized distance between 0.97 and 0.70 is 0.84z (i.e., 0.27/0.32), associated with an area under the "normal" curve (probability) of 0.30. Subtracting this value from 0.50 (assumed proportion of subjects below the mean), yields 0.20, or a childhood prevalence < 0.70 μmol/L of 20%, ~2% above the actual reported prevalence of 17.9% (22). Calculating a normalized estimate from preschooler survey data in Nepal yielded a prevalence of serum retinol < 0.70 μmol/L of 31.7% vs. the reported figure of 32.3% (23). Similar consistency was observed among women. For example, the normalized prevalence of serum retinol < 0.70 μmol/L in Nepalese pregnant women was 26.6 vs. 31.5% reported (23); among Indonesian women, the estimated vs. reported prevalence of low to deficient breast milk vitamin A concentrations (<1.05 μmol/L) was 30.5 vs. 31.0% (24).

Xerophthalmia. In children, estimates of the prevalence of ocular manifestations of VAD were based on reports of reliably diagnosed stages of xerophthalmia, as defined by WHO (21); that is, XN, Bitot's spots (X1B), and active corneal disease (X2 and X3). Data on conjunctival xerosis without X1B (i.e., stage X1A) were not used. Instead of compiling estimates of the burden of separate clinical manifestations of xerophthalmia, a single prevalence of "active xerophthalmia" was derived to estimate the total ocular burden, as done previously (10,11). Thus, where reported, an aggregate rate for all stages of xerophthalmia combined was accepted; where only stage-specific rates were reported, the aggregate rate was usually estimated to be the sum of the prevalence of X2/X3 plus X1B plus one-half the prevalence of XN, assuming that half of all children presenting with Bitot's spots are also night blind. If data were reported for only one ocular manifestation (e.g., either XN or X1B), other stages of xerophthalmia were assumed to be absent.

Among women, estimation of the burden of xerophthalmia was restricted to the most frequently reported symptom, a history of maternal XN. Histories were occasionally reported from cross-sectional assessment (25). However, more often questions about maternal XN covered the entire gestational period of a woman's most recent pregnancy that led to a live birth, either in the preceding 3 y (26) or, as asked in several recent Demographic Health Surveys (DHS),[6] the preceding 5 y. During 7 of 8 national DHS (Ethiopia,

[5] CIC evidence includes that based on use of impression cytology with transfer (ICT) modification on which CIC-abnormality estimates in Africa rely (for example, see references 14,15).

[6] Series of nationally representative surveys coordinated by Macro International Inc., 11785 Beltsville Drive, Calverton, MD 20705 (www.measuredhs.org),

Madagascar, Malawi, Rwanda, Uganda, Zimbabwe and Peru) carried out between 1997 and 2000, questions were asked about both XN and day vision problems during pregnancy (27). Percentages of women reporting to have been night blind from these surveys were adjusted downward by the proportion of surveyed non-XN women who reported having had daytime vision problems during pregnancy (3–16% of all respondents) as a provisional way to reduce, although probably not eliminate, the contribution of potential false positives to estimates of maternal XN.[7]

Data on the above indicators thus provide estimates of prevalence and population burden for two levels of the VAD continuum: low plasma or tissue retinol levels and xerophthalmia (Fig. 1).

Direct estimation of prevalence

Prevalence rates stated to have been obtained from national samples by original investigators, the MDIS (11,12) or MI (10) were accepted as representing a country's entire population of that age.[8] Where countrywide data existed, the number of deficient persons was obtained by multiplying the country's population of preschool-aged children or the number of pregnancies for 1999 (13) by the "national" reported prevalence. Rates based on subnational samples (e.g., surveys conducted in high-risk or other select populations) were adjusted before being used to calculate the national burden of deficiency, as before (10,11), by applying fractional weights to estimate the size of the population represented by these specially selected populations. These adjustments necessarily relied on evidence of representativeness of the surveys and additional risk factor information about a country but were ultimately subjective. Thus, country-specific weights for the size of the "at-risk" population to which the prevalence rates were applied differ from those applied previously for some countries (11,28), based either on new country findings or, at times, after reinterpretation and refinement of earlier data.[9]

Estimates in this article attempt to reflect the impact of VAD prevention programs, implemented after the prevalence surveys were conducted, on the extent of the problem. Program impact varies by mode, dosage, frequency, coverage and sustainability of vitamin A delivery, responsiveness of status indicators and other health factors (29,30). For example, the prevalence of a serum retinol concentration < 0.70 μmol/L decreases by only ~15% in a sustained manner (e.g., for $\geq$2 months) after large-dose vitamin A supplementation (1,23,29,31,32) even in the presence of substantial persistent protection against mortality and xerophthalmia (1,33). High-potency vitamin A is ~90% efficacious in preventing xerophthalmia (29,34,35) and 60–80% effective in programs that achieve reasonably high coverage (23,29,36–38). Thus, childhood VAD and xerophthalmia rates were reduced by 15 and 60%, respectively, in countries reporting sustained postsurvey vitamin A supplementation coverage of $\geq$ 75% (13,27,28,39,40). Although serum retinol and xerophthalmia both respond to an adequate intake of vitamin A-fortified food (41–44), few national fortification programs are under way: none where xerophthalmia is a public health problem and in only one country where fortification seemed to have been substantially launched after its most recent vitamin A survey. In El Salvador, a weight of 0.60 was applied to the national VAD prevalence of 36%, reported in 1988 (45) before sugar fortification was fully implemented, yielding a program-adjusted rate of 21.6%. Prevalence rates obtained during years when there was ongoing, national vitamin A supplementation (e.g., Bangladesh, India, Indonesia) or food fortification with vitamin A (e.g., Honduras and Guatemala) (45,46) were assumed to reflect that program's impact and were not adjusted.

Extrapolation of prevalence

The validity of a global burden estimate relies on completeness of data. However, clinical, biochemical or cytological data of sufficient quality to estimate national burden are lacking for many countries where dietary, demographic and cultural factors suggest that VAD is likely to be a public health problem. For such high-risk countries, the extent of deficiency was extrapolated by one of several approaches, depending on the availability of indicator data from countries elsewhere in the same region.

I. Within the joint WHO African and Eastern Mediterranean Regions, several approaches were adopted:
   A. For 21 countries lacking biochemical or cytological vitamin A status data and classified by WHO as being at "high or very high risk" with respect to child and adult mortality,[10] a prevalence of 28% was imputed. This value represents the 50th percentile of adjusted, national prevalence rates assessed in 33 other countries in both regions (interquartile range of the prevalence distribution: 18.4–49.8%).
   B. For 21 high or very high risk countries lacking ophthalmological survey data, a childhood xerophthalmia prevalence of 1.15% was imputed, representing the 50th percentile of the prevalence distribution for 27 countries in the regions (interquartile range: 0.4–1.9%).
   C. A distributional approach was also adopted for imputing prevalences of maternal VAD ($<$0.70 μmol/L) and low to deficient status ($<$1.05 μmol/L) in 35 high-risk countries lacking data. Using the 25th percentile of the adjusted prevalence distribution for 19 countries, prevalences of 9.4 and 20.4% were assigned, respectively. Adopting the quartile value reflects a poorer availability and greater uncertainty of representative data on maternal vitamin A status compared with the extant data on young children.
   D. A highly conservative approach was taken to impute the minimal prevalence of XN during pregnancy in 46 high-risk countries lacking such data. Based on provisional estimates of national prevalence from nine countrywide surveys across both regions—Egypt, Ethiopia, Madagascar,[11] Malawi, Nigeria, Rwanda, Uganda, Zambia and Zimbabwe (27,48)—the calculated 25th percentile prevalence rate of 4%, although potentially appropriate, was believed to be too high to use directly in the absence of more evidence. Therefore, the lowest prevalence in the series, 2.4% in Nigeria (48), was reduced by an additional 10% (2.2%), reflecting the lowest possible prevalence likely, and was used to estimate the numbers of pregnant women who annually experience XN in these 46 countries.

II. A different approach to imputing prevalence was taken in the Southeast Asian and western Pacific regions. Because of fewer, but in some instances large, countries lacking data, rates of VAD were directly extrapolated to countries without sufficient data from neighboring countries that had reliable population-based estimates and shared comparable levels of development (49), health (13), and mortality risk (47). Most relevant to this approach was extrapolation of a childhood VAD prevalence rate for all of India, including areas in which no biochemical or cytological vitamin A status data are available. Review of rural and urban studies of children conducted over the past 15 y indicated a range of prevalence rates for VAD, from over 50% to ~25% (32,50–55) However, the

funded by the U.S. Agency for International Development, Washington DC (www.usaid.gov).

[7] Decreasing the percentage of women reporting XN by the percentage who also reported day vision problems (DVP) led to 44–78% reductions in the prevalence of reported maternal XN in seven DHS surveys (27). This approach assumes an accuracy of 100% in response to the question about DVP and 0% accuracy of an XN response in the presence of reported DVP, neither of which is likely to be true. Assuming comparable rates of DVP in both groups and applying rates seen in non-XN women with women reporting XN represents a compromise until additional data on extent and validity can be obtained.

[8] This approach differs from previous analyses, which down-weighted rates reported to be nationally representative by a multiplication factor of 0.75 (10–12), implying that only three-fourths of a country's population shared risks of deficiency comparable with the national survey sample. Recently, arguments have been raised in favor of discontinuing this "adjustment" (28).

[9] Individual prevalence estimates, weights and technical notes supporting figures used for each country can be viewed at http://www.jhsph.edu/CHN/GlobalVAD.html.

[10] Countries classified by WHO as categories D and E on the WHO comparative risk assessment scale (47).

[11] USAID MOST Project, unpublished data from National Vitamin A Survey, 2001, International Science and Technology Institute (ISTI), Roslyn, VA.

studies were either not population based or were not sufficiently representative for use in estimating overall prevalence in the population of interest. Available estimates did suggest, however, that the prevalence across India as a whole would probably be at least as high as the composite, population-based rate of 30.8% estimated for neighboring Bangladesh, which has an ongoing national vitamin A distribution program that reaches a significant proportion of the target population (56,57). The existence of a substantial VAD problem in India is further supported by reports of widespread deficiency in childhood dietary consumption of vitamin A (58–60) and moderate risk of xerophthalmia (61), which remains the most important cause of pediatric blindness in India (62). Based on the sum of evidence to date, a minimal, conservative VAD prevalence of 30.8% was also assigned to India.

Other countries that provided a base rate for estimating the prevalence of VAD in neighboring states include Viet Nam [prevalence of 11.8% (63), applied to Cambodia and Laos × a weight of 2] and the Federated States of Micronesia (FSM) [prevalence of 49% (64–66), applied to the Marshall Islands and Kiribati, both with a prevalence of xerophthalmia comparable with the FSM (67–69), and to Papua New Guinea, Solomon Islands, Tonga, Tuvalu and Vanuatu, all with much lower rates of xerophthalmia (68), applied with a weight of 0.25].

III. In the WHO region of the Americas, nearly all countries considered to be endemic for VAD have national data on serum retinol for estimating childhood prevalence, except Haiti, which was conservatively assigned a prevalence of 19.6% based on data from the neighboring Dominican Republic (45).

RESULTS

Estimates of prevalence and numbers of cases of VAD and xerophthalmia among preschool-aged children are displayed by region and for selected countries in **Table 1**. The data suggest there are 127.2 million vitamin A-deficient preschool-aged children. This number represents 25% of preschool-aged

TABLE 1

Global prevalence of preschool child vitamin A deficiency and xerophthalmia, with numbers of cases, by region and selected country[1]

		Vitamin A deficient[2]		Xerophthalmia	
Region/country	Population <5 yrs (×10[3])	%	No. (×10[3])	%	No. of cases (×10[3])
Africa	103,934	32.1	33,406	1.53	1,593
Ethiopia (70)	11,032	61.2	6,752	4.80	530
Kenya (10)	4,462	40.6	1,812	2.00	89
Nigeria (48)	17,880	28.1	5,024	1.00	179
Senegal (10, 12)	1,596	34.5	551	0.36	6
South Africa (71, 72)	4,909	33.3	1,635	1.60	79
Other countries[3]	64,055	27.5	17,632	1.11	710
Eastern Mediterranean	59,818	21.2	12,664	0.85	510
Egypt (73)	8,081	11.9	962	0.32	26
Morocco (45)	3,215	25.5	820	0.16	15
Pakistan (74–76)	23,793	24.0	5,710	0.24	57
Sudan (77, 78)	4,162	23.8	991	1.74	72
Other countries[3]	20,567	20.3	4,181	1.65	340
South/Southeast Asia	169,009	33.0	55,812	1.20	2,026
Bangladesh (56, 57, 79, 80)	15,120	30.8	4,649	0.62	94
India (51–55, 58–61, 81)	114,976	30.8	35,355	1.56	1790
Indonesia (82–86)	22,006	57.5	12,653	0.34	75
Nepal (23)	3,485	34.9	1,216	0.60	21
Sri Lanka (87)	1,597	35.3	564	1.60	26
Other countries[3]	11,825	11.6	1,375	0.17	20
Western Pacific	122,006	14.0	17,128	0.18	220
China (88, 89)	97,793	11.7	11,442	0.17	170
Philippines (31)	9,800	38.0	3,724	0.07	7
Viet Nam (63)	8,454	11.8	998	0.20	17
Other countries[3]	5,959	16.2	964	0.44	26
Region of the Americas	47,575	17.3	8,218	0.16	75
Brazil (11)	15,993	13.7	2,187	0.13	20
Guatemala (10, 45)	1,816	13.4	244	0.00	0
Peru (11)	2,898	13.0	377	0.00	0
Other countries[3]	26,868	20.1	5,410	0.20	55
European region					
Macedonia (12)	152	29.5	45	0	0
Total	502,494	25.3	127,273	0.88	4,424

[1] Table excludes the following countries by WHO region, which are classified as "B" or higher according to the WHO Comparative Risk Assessment Index (47) and for which no prevalence data on preschool child vitamin A deficiency or xerophthalmia exist. Eastern Mediterranean: Bahrain, Cyprus, Jordan, Kuwait, Lebanon, Libya, Qatar, Saudi Arabia, Syria, Tunisia, and the United Arab Emirates. Western Pacific: Australia, Brunei Darussalam, Fiji, Japan, Mongolia, Nauru, New Zealand, Niue, Republic of Korea, Samoa, and Singapore. Americas: Antigua and Barbuda, Argentina, Bahamas, Barbados, Canada, Chile, Cuba, Grenada, Guyana, Jamaica, Paraguay, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, United States of America, and Uruguay. European: all countries are excluded except the Former Yugoslav Republic of Macedonia.

[2] Defined by serum retinol <0.70 μmol/L or, occasionally, abnormal conjunctival impression cytology.

[3] Additional country references are located at *http://www.jhsph.edu/CHN/GlobalVAD.html*.

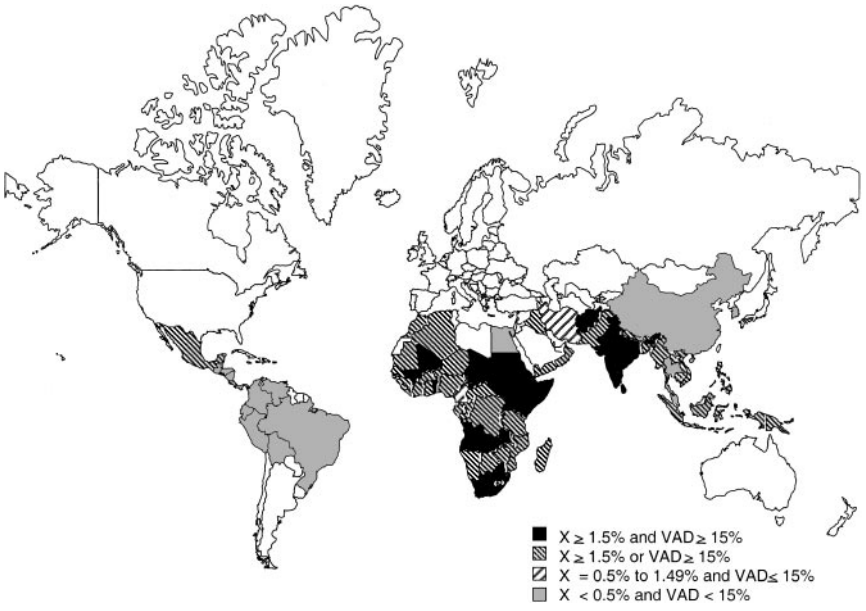

FIGURE 2 Countries stratified by joint prevalence of vitamin A deficiency (VAD), defined by serum retinol concentrations < 0.70 μmol/L or abnormal conjunctival impression cytology, and xerophthalmia (X), all active stages combined, among preschool-aged children.

children in high-risk regions of the developing world, including one developed country destabilized by social conflict. Forty-four percent of vitamin A-deficient children live in South and Southeast Asia, whereas 26 and 10% live in the African and eastern Mediterranean regions, respectively. The largest numbers of vitamin A-deficient children live in India (35.3 million), Indonesia (12.6 million), China (11.4 million), and Ethiopia (6.7 million). Approximately 6.5% (8.2 million) live in the region of the Americas.

Xerophthalmia afflicts 4.4 million preschool-aged children, reflecting 0.9% of all children and 3.5% of all deficient children in these countries. Forty percent of all preschool-aged children with xerophthalmia (1.8 million) in the developing world live in India, a number that also accounts for 88% of all cases in South and Southeast Asia. More than one third of the world's early childhood cases of xerophthalmia (1.6 million) live in Africa, and one third of those reside in Ethiopia (0.53 million). Four percent of the world's xerophthalmic children live in each of three countries: Nigeria, Afghanistan (data not shown), and China.

The global pattern of early childhood risk of VAD and VADD, based on the cutoffs for the prevalence of xerophthalmia (X, all active stages combined) and VAD, is presented in **Figure 2**. The xerophthalmia cutoff of ≥1.5% represents the sum of the minimum prevalence criteria for XN (≥1.0%) and X1B (≥0.5%) considered by WHO to reflect a problem of public health significance (11,21). The cutoff of 0.5% for xerophthalmia corresponds to the minimum public health criterion for X1B (21). The cutoff of ≥ 15% for VAD represents the revised public health minimum prevalence for serum retinol values of <0.70 μmol/L recently adopted by the IVACG (9). The most darkly shaded countries in Figure 2 are those in which the rate of active xerophthalmia is ≥1.5% and the rate of VAD is ≥15%. These are populations in which a high burden of ocular disease emerges from a broad base of childhood VAD. The most lightly shaded countries are those where actual or imputed estimates for xerophthalmia and VAD are both below their respective criteria. Unshaded areas in Africa and the eastern Mediterranean region represent countries classified by WHO as having a low risk of both child and adult mortality (47),[12] lack data on vitamin A status, and are countries where VAD is assumed not to exist.

Table 1 and Figure 2 provide complementary perspectives of the burden of VAD. Countries with prevalence rates below the specified minimum criteria cutoffs may harbor very large numbers of vitamin A-deficient children (e.g., China), whereas others with high prevalence rates may contribute modestly to the global burden (e.g., Haiti). Of potential importance is an emerging pattern in some high-risk countries, such as Bangladesh and Nepal, where periodic high-potency vitamin A delivery seems to be controlling xerophthalmia (23,56) and presumably some of the VAD-induced mortality (1) despite persistent serologic evidence of VAD above the criterion cutoff of 15%.

Table 2 indicates that, among the 107.4 million pregnant women who have a live birth each year in regions of the world at high risk for VAD, 19.8 million (18%) have low to deficient vitamin A status (serum or breast-milk retinol concentrations < 1.05 μmol/L), of whom 7.2 million (37% of those with low status) are deficient (concentrations < 0.70 μmol/L). Of these, 6.2 million women become night blind, assuming that XN occurs only in women with low to deficient vitamin A status (111). This latter estimate suggests that the global burden of maternal XN exceeds that of preschool child xerophthalmia by nearly 50%. About 45% of all pregnant women with low to deficient vitamin A status and over 60% of the cases of maternal XN occurring annually live in South and Southeast Asia; 75% of all regional maternal XN cases (~3 million) are believed to reside in India.

Figure 3 stratifies countries with respect to maternal VAD, restricted to those in which empirical data have been collected for either (or both) serum/breast-milk retinol concentrations (e.g., biochemical) or maternal XN (e.g., clinical). For countries with data for only the biochemical or clinical indicator but not both, estimates are imputed for the other. Countries that lack empirical data for both indicators are not shaded, reflecting the current inadequacy of data on maternal VAD. Thus, Figure 3 is provisional but probably reflects a minimal,

[12] Countries assigned to category B on the comparative risk assessment index (47).

TABLE 2

Global prevalence and annual numbers of cases of maternal vitamin A deficiency and night blindness, by region and selected country[1]

Region/country	Live births per year ($\times 10^3$)	Serum/breast-milk concentration				Night blindness	
		<0.70 μmol/L		<1.05 μmol/L			
		%	No. ($\times 10^3$)	%	No. ($\times 10^3$)	%	No. of cases ($\times 10^3$)
Africa	24,425	10.0	2,452.58	22.0	5,382.72	4.4	1,075.33
Ethiopia (27)	2,699	9.4	253.71	20.4	550.60	16.0	430.76
Kenya (90)	992	9.1	89.88	23.3	230.94	2.2	21.43
Nigeria (91)	4,176	4.7	196.27	10.2	425.95	2.4	100.22
Senegal (11)	364	5.8	21.18	30.6	111.38	2.2	7.86
South Africa (92)	1,055	9.6	100.86	24.4	257.84	2.2	22.79
Other countries[2]	15,139	11.8	1,790.68	25.1	3,806.01	3.3	492.27
Eastern Mediterranean	12,003	7.8	938.35	17.5	2,094.15	3.2	383.79
Egypt (73)	1,720	10.2	175.44	20.4	350.88	9.4	161.68
Morocco (93, 94)	703	12.5	87.88	46.3	325.49	2.2	15.18
Pakistan (11)	5,349	6.4	343.41	12.8	686.81	2.2	115.54
Sudan (11)	944	2.4	22.66	6.4	60.42	2.2	20.39
Other countries[2]	3,287	9.4	308.98	20.4	670.55	2.2	71.00
South/Southeast Asia	36,212	6.2	2,251.39	24.3	8,797.18	10.9	3,930.58
Bangladesh (95–99)	3,504	6.0	210.24	22.5	788.40	12.8	4,485.12
India (100–104)	24,489	4.8	1,175.47	22.8	5,583.49	12.1	2,963.17
Indonesia (105–108)	4,608	10.2	470.02	34.2	1,575.94	6.5	297.22
Nepal (23)	786	31.5	247.59	54.0	424.44	16.7	131.26
Sri Lanka (109)	328	11.6	37.88	27.0	88.56	3.7	12.14
Other countries[2]	2,497	4.4	110.19	13.5	336.35	3.1	78.29
Western Pacific	24,806	5.0	1,239.52	10.9	2,702.33	1.9	466.84
China (88)	19,821	2.0	396.42	4.0	792.94	1.0	198.21
Philippines (11, 31)	2,064	22.2	458.21	44.4	916.42	8.6	177.50
Viet Nam (63)	1,654	15.0	248.10	43.5	719.49	0.7	11.16
Other countries[2]	1,267	10.8	136.79	21.6	273.59	6.3	79.96
Region of the Americas	9,967	3.8	374.78	8.0	799.26	3.8	376.00
Brazil (11)	3,344	2.5	83.60	5.0	167.20	3.7	124.90
Guatemala (110)	399	5.3	20.95	11.3	44.89	1.9	7.45
Peru (27)	610	4.2	25.62	9.0	54.90	7.6	46.38
Other countries[2]	5,614	4.4	244.61	9.5	532.27	3.5	197.27
Total	107,413	6.8	7,256.63	18.4	19,775.63	5.8	6,232.54

[1] Table excludes the following countries by WHO region, which are classified as "B" or higher according to the WHO Comparative Risk Assessment Index (47) and for which no prevalence data on maternal vitamin A deficiency or night blindness exist. Eastern Mediterranean: Bahrain, Cyprus, Iran, Jordan, Kuwait, Lebanon, Libya, Oman Qatar, Saudi Arabia, Syria, Tunisia, and the United Arab Emirates. Western Pacific: Australia, Brunei Darussalam, Fiji, Japan, Mongolia, Nauru, New Zealand, Niue, Republic of Korea, Samoa, and Singapore. Americas: Antigua and Barbuda, Argentina, Bahamas, Barbados, Canada, Chile, Cuba, Grenada, Guyana, Jamaica, Paraguay, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, United States of America, and Uruguay. European: all countries are excluded.

[2] Additional country references can be located at http://www.jhsph.edu/CHN/GlobalVAD.html.

conservative estimate of the global burden. A cutoff of ≥20% for the prevalence of low maternal vitamin A status (serum or breast-milk concentration < 1.05 μmol/L) has been used to classify countries as having a problem in the absence of established cutoffs to define the public health significance by biochemical criteria (16). A maternal XN cutoff of ≥5% has been applied to classify countries, following IVACG's new guidelines (26,112). Countries in which both indicator criteria are currently met, reflecting the heaviest population burden of maternal VAD, include India, Bangladesh, Nepal, Indonesia, Laos, the Philippines, Egypt, Ethiopia, Rwanda, Zambia and Madagascar. Countries of the lightest shade have prevalence rates below both cutoffs.

Available data suggest there is a moderate to severe burden of VAD and VADD among both preschool children and pregnant women, as evidenced by both indicators exceeding criterion cutoffs in India, Ethiopia, Rwanda and Zambia. Lack of empirical data precludes a more comprehensive view of cross-generational VAD.

DISCUSSION

Preschool-aged children

VAD control has been guided by periodic estimates of the numbers of children affected. Early case series and prevalence data collected by Oomen et al. (113), under WHO auspices, brought global attention to xerophthalmia and VAD in children and served as the basis for developing a list of countries likely to be most affected (114); the list continues to be updated today (11,12). Extrapolating population-based data from Indonesia collected in the late 1970s, Sommer et al. (115) conservatively estimated an annual incidence of a half-million cases of potentially blinding corneal disease and ~5 million cases of mild xerophthalmia (XN or X1B) in South and Southeast Asia alone. A decade later, WHO estimated the global burden to be 13 million cases of xerophthalmia and 118–190 million children with biochemical evidence of VAD (116,117). Consistent with this latter range, Humphrey et al.

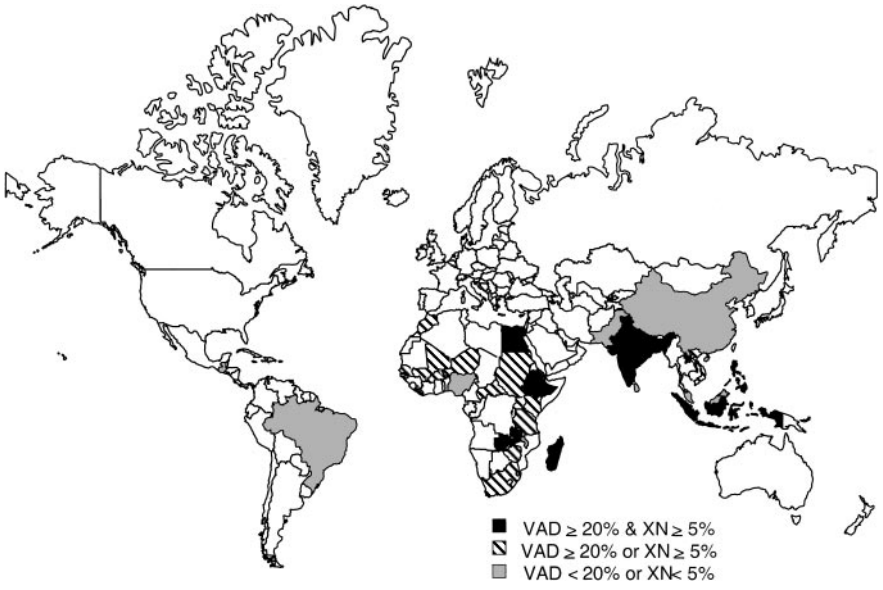

FIGURE 3 Countries stratified by joint prevalence of low to deficient maternal vitamin A status, defined by serum or breast milk retinol concentrations < 1.05 μmol/L and maternal night blindness, based on extant data for either or both indicators. VAD, vitamin A deficiency.

(118) estimated there were 124 million young children with VAD in the developing world at the start of the last decade.

In 1995 however, WHO released a major report on the global prevalence of VAD based on detailed survey findings compiled through its MDIS (11), which reduced the estimated burden of xerophthalmia to 2.8 million preschool children. The seemingly incongruent 80% decrease in the numbers of children with xerophthalmia was consistent, however, with evidence of a declining trend in severe (81,82) and mild (83) xerophthalmia amid intensified vitamin A programming (30) in a number of high-risk countries over the previous several years, motivated by prospects of reducing child mortality (119,120). Given the efficacy of high-potency vitamin A in the treatment (21) and prevention (29) of xerophthalmia, a rapid decline in ocular disease is a plausible response to increased vitamin A coverage in high-risk populations. The apparent decrease in xerophthalmia may also have been due in part to the availability of more accurate prevalence data from the numerous xerophthalmia surveys conducted in the 1980s (78,82,121–124). Paradoxically, however, the 1995 WHO MDIS report estimated the number of VAD preschool-aged children to have nearly doubled, to 254 million (11). In 1998 analysts at Tulane University, UNICEF and the Micronutrient Initiative (10) conducted a multivariate analysis of previous and updated survey findings, concluding that there were 3.3 million children with xerophthalmia, in close agreement with the previous WHO estimate, but only 75–140 million with VAD. The lower limit applied a set of adjustment factors that had been used by WHO to estimate national populations at risk (11), and the upper bound ignored these adjustments. The considerable discrepancy in global burden of vitamin A-deficient children was explained by an error in calculation in the previous WHO report (10).

The present more refined analysis suggests there are 127 million vitamin A-deficient preschool-aged children in the world. This number is about the same as that derived a decade ago (116,118), and it is consistent with the upper, unweighted limit estimated in the MI report (10). However, it exceeds by 70% the lower estimate of 75 million obtained by MI analysts (who applied down-weighted adjustments) (10). Recently, it has been argued that these adjustments, motivated by a concern to provide minimal, conservative estimates, may have led to significant underestimation of the extent of VAD among children (28).

The present analysis suggests that 4.4 million preschool children suffer from clinical xerophthalmia, slightly higher than previous estimates, but arguably within the range of expected variation when calculations are based on different approaches to nonidentical sources of data. In the presence of continued, intensified high-potency vitamin A delivery programs over the past several years (13,28), the slightly higher number may also in part reflect continued population growth.

The map of joint prevalence of childhood VAD and xerophthalmia focuses attention on countries where VAD and its associated disorders are likely to be a severe public health problem. However, the map may also reflect progress in controlling VADD in countries such as Bangladesh, Nepal, Indonesia and the Philippines where the "medium shade" suggests that xerophthalmia is coming under control, and child survival is likely benefitting from high, semiannual coverage with vitamin A supplements, despite persistent hyporetinolemia. The present analysis also suggests that a prevalence cutoff of 1.5% for all active stages of xerophthalmia, representing the sum of established cutoffs for XN (1.0%) and Bitot's spots (0.5%) (21), may be helpful in classifying countries at risk of VADD.

Pregnant women

Historically, maternal VAD has not been recognized as a nutritional problem of public health significance, except in the context of concern about fetal and infant malnourishment with vitamin A (125). This may explain the sparsity of population data on maternal vitamin A status, necessitating reliance in this report on a diverse series of largely nonrepresentative sources of maternal serum and breast milk data, spanning the past 25 y, that included and extended beyond pregnancy and early postpartum periods. Two small studies of maternal XN in India appeared over 3 decades ago (126,127), with little else known about the condition until recently. Evidence of considerable health risks faced by women who experience XN during pregnancy (4,6,111), coupled with the potential to reduce maternal mortality by ensuring an adequate intake of vitamin A during reproductive years (2), has

stimulated recent efforts to assess maternal XN in nationally representative samples of women (23,27,48,95) and led to a history of XN being recommended as a preferred population assessment indicator for maternal and community vitamin A deficiency (9,112).

The present analysis suggests that nearly 20 million pregnant women in the developing world have low vitamin A status; slightly more than one third of them are vitamin A-deficient on biochemical indices, and slightly fewer than one third are clinically night blind. Night-blind women can also be expected to be biochemically vitamin A deficient (111,126,127), which suggests that the latter two groups probably overlap. The analysis suggests that nearly half the estimated 6.2 million annual cases of maternal XN occur in India, a figure that is plausible, because it is based on recent, nationally sampled data (27,128) as well as local area reports (103,129). The new estimates suggest there are nearly 50% more cases of maternal XN than there are preschool children with xerophthalmia in the world, which reflects increasing success in the control of VAD in children and relative neglect among women. The degree to which the present WHO/IVACG recommendation to supplement mothers within 6–8 wk postpartum with 400,000 IU of vitamin A (9), once fully implemented, can also improve control of deficiency among women during pregnancy remains unknown, but it is likely to be inadequate given that early postpartum dosing may provide just enough vitamin A to nourish mother and infant during the first several months of lactation (130,131).

These data on maternal VAD and XN suggest the need to focus more attention on assessment, prevention and control of maternal VAD and its disorders, especially throughout the South and Southeast Asian and African regions. Figure 3, however, also reveals a stark inadequacy of data on maternal vitamin A status in most high-risk countries and the provisional nature of the current estimates. By including questions about maternal XN in the core questionnaires of recent Demographic Health (27) and UNICEF Multiple Indicator Cluster (95) surveys, some critical population data on maternal XN has become available, although there remains a need for further validation studies and biochemical survey data.

VAD remains a major public health concern early in life in most developing regions of the world. Since the early 1980s, VAD prevention programs seem to have reduced the number of xerophthalmic children, and probably attributable blindness and death, and to have curbed further increases in the burden of xerophthalmia and VAD despite considerable population growth. No estimates of global or regional burden exist for school-aged children, nor are the consequences of VADD understood in this age group. However, the present analysis suggests that VAD persists into adulthood, is a major public health problem among women of reproductive age and manifests most clearly during pregnancy and the early postpartum period. Although efforts to reduce the burden of deficiency in preschool children continue, increased attention should be given to defining the extent, severity and health consequences of maternal VAD and its prevention.

ACKNOWLEDGMENTS

I thank Alfred Sommer and Amy Rice for helpful comments and Jonathan Sugimoto for assistance.

LITERATURE CITED

1. Sommer, A. & West, K. P., Jr. (1996) Vitamin A Deficiency: Health, Survival, and Vision. Oxford University Press, New York, NY.

2. West, K. P., Jr., Katz, J., Khatry, S. K., LeClerq, S. C., Pradhan, E. K., Shrestha, S. R., Connor, P. B., Dali, S. M., Christian, P., Pokhrel, R. P. & Sommer, A. (1999) Double blind, cluster randomised trial of low dose supplementation with vitamin A or β-carotene on mortality related to pregnancy in Nepal. The NNIPS-2 Study Group. Br. Med. J. 318: 570–575.

3. Christian, P., West, K. P., Jr., Khatry, S. K., Katz, J., LeClerq, S. C., Kimbrough-Pradhan, E., Dali, S. M. & Shrestha, S. R. (2001) Vitamin A or β-carotene supplementation reduces symptoms of illness in pregnant and lactating Nepali women. J. Nutr. 130: 2675–2682.

4. Christian, P., West, K. P., Jr., Khatry, S. K., Kimbrough-Pradhan, E., LeClerq, S. C., Katz, J., Shrestha, S. R., Dali, S. M. & Sommer, A. (2000) Night blindness during pregnancy and subsequent mortality among women in Nepal: effects of vitamin A and β-carotene supplementation. Am. J. Epidemiol. 152: 542–547.

5. Humphrey, J. H., Agoestina, T., Wu, L., Usman, A., Nurachim, M., Subardja, D., Hidayat, S., Tielsch, J., West, K. P., Jr. & Sommer, A. (1996) Impact of neonatal vitamin A supplementation on infant morbidity and mortality. J. Pediatr. 128: 489–496.

6. Christian, P., West, K. P., Jr., Khatry, S. K., LeClerq, S. C., Kimbrough-Pradhan, E., Katz, J. & Shrestha, S. R. (2001) Maternal night blindness increases risk of infant mortality in the first 6 months of life in Nepal. J. Nutr. 131: 1510–1512.

7. Tielsch, J. M., Rahmathullah, L., Thulasiraj, R. D., Katz, J., Coles, C. & Selvaraj. (2001) Impact of vitamin A supplementation to newborns on early infant mortality: a community-based, randomized trial in South India. XX IVACG meeting, Hanoi, Vietnam.

8. McLaren, D. S. & Frigg, M. (1997) Sight and Life Manual on Vitamin A Deficiency Disorders (VADD), 1st ed. Task Force Sight and Life, Basel, Switzerland.

9. Sommer, A. & Davidson, F. R. (2002) Assessment and control of vitamin A deficiency: the Annecy Accords. J. Nutr. 132: 2845S-2851S.

10. The Micronutrient Initiative. (1998) Progress in Controlling Vitamin A Deficiency. The Micronutrient Initiative, the United Nations Children's Fund, Tulane University, Ottawa, Canada.

11. World Health Organization. (1995) The Global Prevalence of Vitamin A Deficiency. Micronutrient Deficiency Information System (MDIS) Working Paper 2: WHO/NUT/95 3:World Health Organization, Geneva, Switzerland.

12. World Health Organization. (2001) Vitamin A Deficiency & Iodine Deficiency Disorders Prevalence Estimates for the Global Burden of Disease, Micronutrient Deficiency Information System (MDIS). World Health Organization, Geneva, Switzerland.

13. United Nations Children's Fund. (2001) The State of the World's Children 2001. UNICEF, New York, NY.

14. Carlier, C., Moulia-Pelat, J. P., Ceccon, J. F., Mourey, M. S., Ameline, B., Fall, M., N'Diaye, M. & Amedee-Manesme, O. (1991) Prevalence of malnutrition and vitamin A deficiency in the Diourbel, Fatick, and Kaolack regions of Senegal: epidemiological study. Am. J. Clin. Nutr. 53: 70–73.

15. Resnikoff, S., Filliard, G., Carlier, C., Luzeau, R. & Amedee-Manesme, O. (1992) Assessment of vitamin A deficiency in the Republic of Djibouti. Eur. J. Clin. Nutr. 46: 25–30.

16. World Health Organization. (1996) Indicators for Assessing Vitamin A Deficiency and Their Application in Monitoring and Evaluating Intervention Programmes. Report No. WHO/NUT/96 10: World Health Organization, Geneva, Switzerland.

17. Stoltzfus, R. J. & Underwood, B. A. (1995) Breast-milk vitamin A as an indicator of the vitamin A status of women and infants. Bull. WHO 73: 703–711.

18. Natadisastra, G., Wittpenn, J. R., West, K. P., Muhilal & Sommer, A. (1987) Impression cytology for detection of vitamin A deficiency. Arch. Ophthalmol. 105: 1224–1228.

19. Amedee-Manesme, O., Luzeau, R., Wittpenn, J. R., Hanck, A., & Sommer, A. (1988) Impression cytology detects subclinical vitamin A deficiency. Am. J. Clin. Nutr. 47: 875–878.

20. Reddy, V., Rao, V. & Arunjyothi, Reddy, M. (1989) Conjunctival impression cytology for assessment of vitamin A status. Am. J. Clin. Nutr. 50: 814–817.

21. Sommer, A. (1995) Vitamin A Deficiency and Its Consequences. A Field Guide to Detection and Control, 3rd ed. World Health Organization, Geneva, Switzerland.

22. Jervis, R., Rodrugues, A. & Nelson, D. (1994) Vitamin A deficiency in Ecuador. Nutriview 4: 2–3.

23. Nepal Micronutrient Status Survey. (1998) Ministry of Health, Child Health Division, His Majesty's Government of Nepal; New ERA, Micronutrient Initiative, UNICEF Nepal; and WHO, Kathmandu, Nepal.

24. Stoltzfus, R. J., Hakimi, M., Miller, K. W., Rasmussen, K. M., Dawiesah, S., Habicht, J. P. & Dibley, M. J. (1993) High dose vitamin A supplementation of breast-feeding Indonesian mothers: effects on the vitamin A status of mother and infant. J. Nutr. 123: 666–675.

25. Luo, C., Mwela, C., Foote, D., Kafwimbe, E. & Schultz, K. (1999) National vitamin A deficiency prevalence survey in Zambia. XIX IVACG Meeting, Durban, South Africa.

26. Christian, P. (2002) Recommendations for indicators: night blindness during pregnancy—a simple tool to assess vitamin A deficiency in a population. J. Nutr. 132: 2884S–2888S.

27. Micronutrient Update. (2001) Measure DHS+, ORC Macro, Calverton, MD.

28. Mason, J. B., Lotfi, M., Dalmiya, N., Sethuraman, K. & Deitchler, M. (2001) The Micronutritient Report. Current Progress and Trends in the Control of Vitamin A, Iodine, and Iron Deficiencies. The Micronutrient Initiative, Ottawa, Ontario, Canada.

29. West, K. P., Jr. & Sommer, A. (1987) Delivery of Oral Doses of Vitamin A

to Prevent Vitamin A Deficiency and Nutritional Blindness. ACC/SCN State-of-the-Art Series, Nutrition Policy Discussion Paper No. 2: ACC/SCN, Rome, Italy.

30. Gillespie, S. & Mason, J. (1994) Controlling Vitamin A Deficiency. ACC/SCN State-of-the-Art series Nutrition Policy Discussion Paper No. 14. Report based on the ACC/SCN Consultative Group Meeting on Strategies for the Control of Vitamin A Deficiency, Ottawa, Canada, 1993. Administrative Committee on Coordination/Subcommittee on Nutrition, Geneva, Switzerland.

31. Villavieja, G. M., Palafox, E. F., Cerdena, C. M., Lana, R. D., de los Reyes, C. M. & Shekar, M. (1999) Initial results of the fifth national nutrition survey: Philippines, 1998. Food and Nutrition Research Institute, Taguig, the Philippines.

32. Rahmathullah, L. (1991) Effect of receiving a weekly dose of vitamin A equivalent to the recommended dietary allowances among pre school children on mortality in south India. Indian J. Pediatr. 58: 837–847.

33. Beaton, G. H., Martorell, R., Aronson, K. J., Edmonston, B., McCabe, G., Ross, A. C. & Harvey, B. (1993) Effectiveness of vitamin A supplementation in the control of young child morbidity and mortality in developing countries. ACC/SCN State-of-the-Art Series Nutrition Policy Discussion Paper No. 13: Administrative Committee on Coordination/Subcommittee on Nutrition (ACC/SCN), Geneva, Switzerland.

34. Vijayaraghavan, K., Sarma, K. V., Rao, N. P. & Reddy, V. (1984) Impact of massive doses of vitamin A on incidence of nutritional blindness. Lancet 2: 149–151.

35. Katz, J., West, K. P., Jr., Khatry, S. K., Thapa, M. D., LeClerq, S. C., Pradhan, E. K., Pokhrel, R. P. & Sommer, A. (1995) Impact of vitamin A supplementation on prevalence and incidence of xerophthalmia in Nepal. Invest. Ophthalmol. Vis. Sci. 36: 2577–2583.

36. Djunaedi, E., Sommer, A., Pandji, A., Kusdiono & Taylor, H. R. (1988) Impact of vitamin A supplementation on xerophthalmia. A randomized controlled community trial. Aceh Study Group. Arch. Ophthalmol. 106: 218–222.

37. Cohen, N., Rahman, H., Mitra, M., Sprague, J., Islam, S., Leemhuis de Regt, E. & Jalil, M. A. (1987) Impact of massive doses of vitamin A on nutritional blindness in Bangladesh. Am. J. Clin. Nutr. 45: 970–976.

38. Bloem, M. W., Hye, A., Wijnroks, M., Ralte, A., West, K. P., Jr. & Sommer, A. (1995) The role of universal distribution of vitamin A capsules in combatting vitamin A deficiency in Bangladesh. Am. J. Epidemiol. 142: 843–855.

39. Pan American Health Organization. Vitamin A supplementation coverage table in The Americas, 1999. http://www.paho.org (Quick Search: vitamin A) (accessed July 22, 2002).

40. Goodman, T., Dalmiya, N., de Benoist, B. & Schultink, W. (2000) Polio as a platform: using national immunization days to deliver vitamin A supplements. Bull. WHO 78: 305–314.

41. Solon, F. S., Klemm, R. D., Sanchez, L., Darnton-Hill, I., Craft, N. E., Christian, P. & West, K. P., Jr. (2000) Efficacy of a vitamin A-fortified wheat-flour bun on the vitamin A status of Filipino schoolchildren. Am. J. Clin. Nutr. 72: 738–744.

42. Arroyave, G., Aguilar, J. R., Flores, M. & Guzman, M. (1979) Evaluation of Sugar Fortification with Vitamin A at the National Level. Scientific Publication 384: Pan American Health Organization, Washington, DC.

43. Muhilal, Murdiana, A., Azis, I., Saidin, S., Jahari, A. B. & Karyadi, D. (1988) Vitamin A-fortified monosodium glutamate and vitamin A status: a controlled field trial. Am. J. Clin. Nutr. 48: 1265–1270.

44. Solon, F. S., Solon, M. S., Mehansho. H., West. K. P., Jr., Sarol, J., Perfecto, C., Nano, T., Sanchez, L., Isleta, M., Wasantwisut, E. & Sommer, A. (1996) Evaluation of the effect of vitamin A fortified margarine on the vitamin A status of preschool Filipino children. Eur. J. Clin. Nutr. 50: 720–723.

45. Administrative Committee on Coordination/Subcommittee on Nutrition. (1997) Report on the World Nutrition Situation. Third Report on the World Nutrition Situation. ACC/SCN, Geneva, Switzerland.

46. Pineda, R. R. (1998) World Relief (Auxilio Mundial) Honduras (WRH) Child Survival Project—El Paraiso. Sight and Life Newsletter 1: 11–12.

47. World Health Organization. (2000) The World Health Report 2000. Health Systems: Improving Performance. World Health Organization, Geneva, Switzerland.

48. Opportunities for Micronutrient Interventions. (1993) National Micronutrient Survey, Nigeria. OMNI, University of Ibadan, USAID, Washington, DC.

49. United Nations Development Programme (UNDP). (1999) Human Development Report 1999. Oxford University Press, New York, NY.

50. Bhaskaram, P., Balakrishna, N., Madhavan Nair, K. & Sivakumar, B. (2000) Vitamin A deficiency in infants: effects of postnatal maternal vitamin A supplementation on the growth and vitamin A status. Nutr. Res. 20: 769–778.

51. Reddy, V., Raghuramulu, N., Arunjyothi, Shivaprakash, M. & Underwood, B. A. (1986) Absorption of vitamin A by children with diarrhoea during treatment with oral rehydration salt solution. Bull. WHO 64: 721–724.

52. Pant, I. & Gopaldas, T. (1987) Effect of mega doses of vitamin A on the vitamin A status of underprivileged school-age boys (7–15 yr). Indian J. Med. Res. 86: 196–206.

53. Usha, N., Sankaranarayanan, A., Walia, B. N. & Ganguly, N. K. (1991) Assessment of preclinical vitamin A deficiency in children with persistent diarrhea. J. Pediatr. Gastroenterol. Nutr. 13: 168–175.

54. Bhandari, N., Bhan, M. K. & Sazawal, S. (1994) Impact of massive dose of vitamin A given to preschool children with acute diarrhoea on subsequent respiratory and diarrhoeal morbidity. Br. Med. J. 309: 1404–1407.

55. Sanchez, A. M., Congdon, N. G., Sommer, A., Rahmathullah, L., Venkataswamy, P. G., Chandravathi, P. S. & Clement, L. (1997) Pupillary threshold as an index of population vitamin A status among children in India. Am. J. Clin. Nutr. 65: 61–66.

56. Helen Keller International, Bangladesh. (2001) The Nutritional Surveillance Project in Bangladesh in 1999. Towards the Goals of the 1990 World Summit for Children. Helen Keller International, Dhaka, Bangladesh.

57. Hussain, A., Kvale, G. & Odland, M. (1995) Diagnosis of night blindness and serum vitamin A level: a population-based study. Bull. WHO 73: 469–476.

58. Khandait, D. W., Vasudeo, N. D., Zodpey, S. P., Ambadekar, N. N. & Koram, M. R. (1999) Vitamin A intake and xerophthalmia among Indian children. Publ. Health 113: 69–72.

59. Ramakrishnan, U., Martorell, R., Latham, M. C. & Abel, R. (1999) Dietary vitamin A intakes of preschool-age children in South India. J. Nutr. 129: 2021–2027.

60. National Nutrition Monitoring Bureau, Government of India. (2000) Report on Nutritional Status of the Rural Population, 1996, summarized in background document for the National Consultation on Vitamin A, September 29–30, 2000. National Nutrition Monitoring Bureau, Government of India, New Delhi, India.

61. Department of Women and Child Development. (1998) India Nutrition Profile. Ministry of Human Resource Development, Government of India, New Delhi, India.

62. Rahi, J. S., Sripathi, S., Gilbert, C. E. & Foster, A. (1995) Childhood blindness due to vitamin A deficiency in India: regional variations. Arch. Dis. Child. 72: 330–333.

63. Khan, N. C. (2001) Evolution, impact and future of the Vietnam vitamin A programme. VAD control programme in Vietnam: situation, policy and programme. Sight and Life Newsletter 1: 8–9.

64. Centers for Disease Control and Prevention. (2001) Vitamin A deficiency among children—Federated States of Micronesia, 2000. MMWR Morb. Mortal Wkly. Rep. 50: 509–512.

65. Lloyd-Puryear, M., Humphrey, J. H., West, K. P., Jr., Aniol, K., Mahoney, F., Mahoney, J. & Keenum, D. G. (1989) Vitamin A deficiency and anemia among Micronesian children. Nutr. Res. 9: 1007–1016.

66. Lloyd-Puryear, M. A., Mahoney, J., Humphrey, J. H., Mahoney, F., Siren, N., Moorman, C. & West, K. P., Jr. (1991) Vitamin A deficiency in Micronesia: a statewide survey in Chuuk. Nutr. Res. 11: 1101–1110.

67. Danks, J., Kaufman, D. & Rait, J. (1992) A clinical and cytological study of vitamin A deficiency in Kiribati. Aust. N. Z. J. Ophthalmol. 20: 215–218.

68. Schaumberg, D. A., Linehan, M., Hawley, G., O'Connor, J., Dreyfuss, M. & Semba, R. D. (1995) Vitamin A deficiency in the South Pacific. Publ. Health 109: 311–317.

69. Schaumberg, D. A., O'Connor, J. & Semba, R. D. (1996) Risk factors for xerophthalmia in the Republic of Kiribati. Eur. J. Clin. Nutr. 50: 761–764.

70. Haidar, J. & Demissie, T. (1999) Malnutrition and xerophthalmia in rural communities of Ethiopia. E. Afr. Med. J. 76: 590–593.

71. South African Vitamin A Consultative Group. (1996) The vitamin A status of South African children 6–71 months of age: results of the national survey. Proceedings of the XVII IVACG meeting, Guatemala City, March 18–22, 1996. International Life Sciences Institute, Washington, DC.

72. South African Vitamin A Consultative Group. (1996) Child malnutrition in South Africa. Nutriview 1: 1–3.

73. Moussa, W., Shaheen, F. M., ElNahry, F. I., Abdel Gilil, A. M., Noor, E. F., Darwish, A. A., Michael, N. A., Hassanyn, S. A., Tawfik, A. A., Nasr, F. A. & Youssef, A. N. (1997) Vitamin A status in Egypt. Proceedings of the XVIII IVACG Meeting, Cairo, Egypt, 22–26 September 1997: International Life Sciences Institute, Washington, DC.

74. Paracha, P. I., Jamil, A., Northrop-Clewes, C. A. & Thurnham, D. I. (2000) Interpretation of vitamin A status in apparently healthy Pakistani children by using markers of subclinical infection. Am. J. Clin. Nutr. 72: 1164–1169.

75. Paracha, P. I. & Jameel, A. (2000) Vitamin A deficiency and infection in Pakistani preschool children. Sight and Life Newsletter 1: 25–26.

76. Khan, M. M., Abbas, S. & Abbas, K. A. (1988) Vitamin A Status of Pre-school Children in Islamabad. Pakistan Institute of Medical Sciences, Islamabad, Pakistan.

77. Nestel, P., Herrera, M. G., El Amin, A., Fawzi, W., Mohammed, K. A. & Weld, L. (1993) Risk factors associated with xerophthalmia in northern Sudan. J. Nutr. 123: 2115–2121.

78. El Bushra, H. E. & El Tom, A. R. (1987) Vitamin A deficiency: a public health problem in eastern Sudan. E. Afr. Med. J. 64: 782–789.

79. Helen Keller International, Institute of Nutrition and Food Science. (1999) Vitamin A status throughout the lifecycle in rural Bangladesh. National vitamin A survey 1997–1998. Sight and Life Newsletter 4: 26–29.

80. Helen Keller International, Bangladesh. (1999) Vitamin A Status throughout the lifecycle in rural Bangladesh. National Vitamin A Survey 1997- 98: Helen Keller International, Dhaka, Bangladesh.

81. Rahmathullah, L., Paul Raj, M. S. & Chandravathi, T. S. (1997) Aetiology of severe vitamin A deficiency in children. Nat. Med. J. India 10: 62–64.

82. Semba, R. D., Susatio, B., Muhilal & Natadisastra, G. (1995) The decline of admissions for xerophthalmia at Cicendo Eye Hospital, Indonesia, 1981–1992. Int. Ophthalmol. 19: 39–42.

83. Muhilal, Tarwotjo, I., Kodyat, B., Herman, S., Permaesih, D., Karyadi, D., Wilbur, S. & Tielsch, J. M. (1994) Changing prevalence of xerophthalmia in Indonesia, 1977–1992. Eur. J. Clin. Nutr. 48: 708–714.

84. Tanumihardjo, S. A., Permaesih, D., Muherdiyantiningsih, Rustan, E., Rusmil, K., Fata, A. C., Wilbur, S., Muhilal, Karyadi, D. & Olson, J. A. (1996) Vitamin A status of Indonesian children infected with *Ascaris lumbricoides* after dosing with vitamin A supplements and albendazole. J. Nutr. 126: 451–457.

85. Tarwotjo, I., Tilden, R., Farida, Atmarita, Grosse, R., Sommer, A., Perry, B. & Richlen-Tilden, K. (1989) The change of prevalence of xerophthalmia on Lombok, September 1977–September 1983. Penelitian Gizi Dan Makanan 12: 1–11.

86. Kjolhede, C. L., Stallings, R. Y., Dibley, M. J., Sadjimin, T., Dawiesah, S. &

Padmawati, S. (1995) Serum retinol levels among preschool children in central Java: demographic and socioeconomic determinants. Int. J. Epidemiol. 24: 399–403.

87. Piyasema, C. L., Mahanithawa, A. & De Silva, S. (1999) Prevalence of vitamin A deficiency in Sri Lanka. Proceedings of the XIX IVACG Meeting, Durban, South Africa, 8–11 March 1999: International Life Sciences Institute, Washington, DC.

88. Yan, L. (2001) Recent survey on children with vitamin A deficiency in China. Sight and Life Newsletter 2: 37–39.

89. Yip, R. (2000) 2000 China National Vitamin A Survey. UNICEF, New York, NY.

90. Mostad, S. B., Overbaugh, J., DeVange, D. M., Welch, M. J., Chohan, B., Mandaliya, K., Nyange, P., Martin, H. L., Jr., Ndinya-Achola, J., Bwayo, J. J. & Kreiss, J. K. (1997) Hormonal contraception, vitamin A deficiency, and other risk factors for shedding of HIV-1 infected cells from the cervix and vagina. Lancet 350: 922–927.

91. Ette, S. I. & Esenowo, E. J. (1986) Plasma concentrations of retinol and vitamins E and C during the first twelve months of postnatal life. Trop. Geogr. Med. 38: 1–5.

92. Fairney, A., Sloan, M. A., Patel, K. V. & Coumbe, A. (1987) Vitamin A and D status of black South African women and their babies. Hum. Nutr. Clin. Nutr. 41C: 81–87.

93. Mokhtar, N. (1998) Vitamin A situation of reproductive age women in the Gharb region of Morocco: findings from a regional study. OMNI/USAID Report, International Science and Technology Institute (ISTI), Rosslyn, VA.

94. Mokhtar, N., Belahsen, B., Nasri, I. & Aguenaou, H. (1997) Vitamin A deficiency prevalence in women from 15 to 49 years in two agricultural communities in Morocco. Proceedings of the XVIII IVACG Meeting, Cairo, Egypt, 22–26 September 1997: International Life Sciences Institute, Washington, DC.

95. UNICEF, Progotir Pathey. (1998) Achieving the Goals for Children in Bangladesh. Bangladesh Bureau of Statistics, Ministry of Planning, Government of the People's Republic of Bangladesh, and UNICEF, Dhaka, Bangladesh.

96. Ahmed, F., Khan, M. R., Karim, R., Taj, S., Hyderi, T., Faruque, M. O. & Margetts, B. M. (1996) Serum retinol and biochemical measures of iron status in adolescent schoolgirls in urban Bangladesh. Eur. J. Clin. Nutr. 50: 346–351.

97. Ahmed, F., Hasan, N. & Kabir, Y. (1997) Vitamin A deficiency among adolescent female garment factory workers in Bangladesh. Eur. J. Clin. Nutr. 51: 698–702.

98. Kolsteren, P., Rahman, S. R., Hilderbrand, K. & Diniz, A. (1999) Treatment for iron deficiency anaemia with a combined supplementation of iron, vitamin A and zinc in women of Dinajpur, Bangladesh. Eur. J. Clin. Nutr. 53: 102–106.

99. Rice, A. L., Stoltzfus, R. J., de Francisco, A., Chakraborty, J., Kjolhede, C. L. & Wahed, M. A. (1999) Maternal vitamin A or β-carotene supplementation in lactating Bangladeshi women benefits mothers and infants but does not prevent subclinical deficiency. J. Nutr. 129: 356–365.

100. Shah, R. S. & Rajalakshmi, R. (1984) Vitamin A status of the newborn in relation to gestational age, body weight, and maternal nutritional status. Am. J. Clin. Nutr. 40: 794–800.

101. Sivakumar, B., Panth, M., Shatrugna, V. & Raman, L. (1997) Vitamin A requirements assessed by plasma response to supplementation during pregnancy. Int. J. Vit. Nutr. 67: 232–236.

102. Shatrugna, V., Raman, L., Uma, K. & Sujatha, T. (1997) Interaction between vitamin A and iron: effects of supplements in pregnancy. Int. J. Vit. Nutr. Res. 67: 145–148.

103. Kapil, U., Pathak, P., Tandon, M., Singh, C., Pradhan, R. & Dwivedi, S. N. (1999) Micronutrient deficiency disorders amongst pregnant women in three urban slum communities of Delhi. Indian Pediatr. 36: 983–989.

104. Ganguly, C. & Mukherjee, K. L. (1988) Relationship between maternal serum vitamin A and vitamin A status of the corresponding fetuses. J. Trop. Pediatr. 34: 313–315.

105. Suharno, D., West, C. E., Muhilal, Karyadi, D. & Hautvast, J. G. (1993) Supplementation with vitamin A and iron for nutritional anaemia in pregnant women in West Java, Indonesia. Lancet 342: 1325–1328.

106. Tanumihardjo, S. A., Muherdiyantiningsih, Permaesih, D., Domala, Muhilal, Karyadi, D. & Olson, J. A. (1996) Daily supplements of vitamin A (8.4 μmol, 8000 IU) improve the vitamin A status of lactating Indonesian women. Am. J. Clin. Nutr. 63: 32–35.

107. de Pee, S., Yuniar, Y., West, C. E. & Muhilal. (1997) Evaluation of biochemical indicators of vitamin A status in breast-feeding and non-breast-feeding Indonesian women. Am. J. Clin. Nutr. 66: 160–167.

108. Stoltzfus, R. J., Hakimi, M., Miller, K. W., Rasmussen, K. M., Dawiesah, S., Habicht, J. P. & Dibley, M. J. (1993) High dose vitamin A supplementation of breast-feeding Indonesian mothers: effects on the vitamin A status of mother and infant. J. Nutr. 123: 666–775.

109. Jayasekera, J. P., Atukorala, T. M. & Seneviratne, H. R. (1991) Vitamin A status of pregnant women in five districts of Sri Lanka. Asia-Oceania J. Obstet. Gynaecol. 17: 217–224.

110. Arroyave, G., Aguilar, J. R., Flores, M. & Guzman, M. A. (1979) Evaluation of sugar fortification with vitamin A at the national level. PAHO Scientific Publication No. 384, pp. 1–82. Pan American Health Organization, Washington, DC.

111. Christian, P., West, K. P., Jr., Khatry, S. K., Katz, J., Shrestha, S. R., Pradhan, E. K., LeClerq, S. C. & Pokhrel, R. P. (1998) Night blindness of pregnancy in rural Nepal—nutritional and health risks. Int. J. Epidemiol. 27: 231–237.

112. Christian, P. (2002) Maternal Night Blindness: A New Indicator of Vitamin A Deficiency. IVACG Statement. International Vitamin A Consultative Group, Washington, DC.

113. Oomen, H. A., McLaren, D. S. & Escapini, H. (1964) Epidemiology and public health aspects of hypovitaminosis A. A global survey of xerophthalmia. Trop. Geogr. Med. 4: 271–315.

114. Protein Advisory Group. (1976) Vitamin A enrichment of donated foods. PAG Bull. 6: 1–7.

115. Sommer, A., Tarwotjo, I., Hussaini, G., Susanto, D. & Soegiharto, T. (1981) Incidence, prevalence, and scale of blinding malnutrition. Lancet 1: 1407–1408.

116. World Health Organization. (1992) National Strategies for Overcoming Micronutrient Malnutrition. Forty-fifth World Health Assembly, WHO A45/17. World Health Organization, Geneva, Switzerland.

117. Underwood, B. A. (1994) Vitamin A in human nutrition. Public health considerations. In: The Retinoids: Biology, Chemistry, and Medicine, Vol. 4, 2nd ed. (Sporn, M. B., Roberts, A. B. & Goodman, D. S., eds.), pp. 211–227. Raven Press, New York, NY.

118. Humphrey, J. H., West, K. P., Jr. & Sommer, A. (1992) Vitamin A deficiency and attributable mortality among under-5-year-olds. Bull. WHO 70: 225–232.

119. Sommer, A., Tarwotjo, I., Djunaedi, E., West, K. P., Jr., Loedin, A. A., Tilden, R. & Mele, L. (1986) Impact of vitamin A supplementation on childhood mortality: a randomized controlled community trial. The Aceh Study Group. Lancet 1: 1169–1173.

120. Administrative Committee on Coordination/Subcommittee on Nutrition. (1986) UN-ACC Subcommittee on Nutrition: Statement on vitamin A and mortality. Twelfth session of the SCN, Tokyo, April 7–11, 1986. Food Nutr. Bull. 8: 65.

121. Tielsch, J. M., West, K. P., Jr., Katz, J., Chirambo, M. C., Schwab, L., Johnson, G. J., Tizazu, T., Swartwood, J. & Sommer, A. (1986) Prevalence and severity of xerophthalmia in southern Malawi. Am. J. Epidemiol. 124: 561–568.

122. Sukwa, T., Mwandu, D., Kapui, A., Siziya, S., Vamoer, A., Mukunyandela, M. & Chelemu, V. (1988) The prevalence and distribution of xerophthalmia in pre-school age-children of the Luapula Valley, Zambia. J. Trop. Pediatr. 34: 12–15.

123. Wolde-Gebriel, Z., Demeke, T. & West, C. E. (1991) Xerophthalmia in Ethiopia: a nationwide ophthalmological, biochemical and anthropometric survey. Eur. J. Clin. Nutr. 45: 469–478.

124. Bonnet, S., Resnikoff, S., Castan, R., Konate, S., Periquet, B., Coste, J. & Amedee-Manesme, O. (1992) Assessment of vitamin A deficiency in a rural area in Mali. Estimation of sample size for the impression cytology test. Int. J. Vit. Nutr. Res. 62: 291–297.

125. Underwood, B. A. (1994) Maternal vitamin A status and its importance in infancy and early childhood. Am. J. Clin. Nutr. 59: 517S–524S.

126. Dixit, D. T. (1966) Night-blindness in third trimester of pregnancy. Indian J. Med. Res. 54: 791–795.

127. Mandal, G. S., Nanda, K. N. & Bose, J. (1969) Night blindness in pregnancy. J. Obstet. Gynecol. India 19: 453–458.

128. U.S. Agency for International Development. (2000) Benefits and safety of administration of synthetic vitamin A to children. Background document for the National Consultation on Vitamin A, September 29–30, 2000. U.S. Agency for International Development, Washington, DC.

129. Patel, D. (1999) Prevalence of nightblindness during pregnancy in a tribal community of Gujarat. ARCH Working Paper: Action Research in Community Health and Development, Bharuch, Gujarat, India.

130. Allen, L. H. & Haskell, M. (2001) Vitamin A requirements of infants under six months of age. Food Nutr. Bull. 22: 214–234.

131. Humphrey, J. H. & Rice, A. L. (2000) Vitamin A supplementation of young infants. Lancet 356: 422–424.