AGENCY FOR INTERNATIONAL DEVELOPMENT
WASHINGTON, D. C. 20523

BIBLIOGRAPHIC INPUT SHEET

FOR AID USE ONLY

1. SUBJECT CLASSIFICATION

A. PRIMARY: Public Health

B. SECONDARY: Nutrition

2. TITLE AND SUBTITLE

Vitamin A Problems with Special Reference to Less Developed Countries-Volume II

3. AUTHOR(S)

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4. DOCUMENT DATE	5. NUMBER OF PAGES	6. ARC NUMBER
July 1973	62p.	ARC

7. REFERENCE ORGANIZATION NAME AND ADDRESS

Agency for International Development
Office of Nutrition
Washington, D.C. 20523

8. SUPPLEMENTARY NOTES *(Sponsoring Organization, Publishers, Availability)*

9. ABSTRACT

Vitamin A deficiency is known to be a problem of major public health significance in a number of less developed countries. In its acute form in young children it leads to partial or total blindness and thus has widespread economic and social implications. Not enough is known about the extent and seriousness of less acute forms of hypovitaminosis A. The problem as a whole is commanding increasing interest and attention.

This "position paper" is a contribution to CDC-AID efforts to delineate the problems and the possibilities for concrete assistance. In the course of preparing the report, discussions were held with FAO nutrition staff in Rome, and WHO nutrition staff in Geneva.

10. CONTROL NUMBER

PN-AAB-387

11. PRICE OF DOCUMENT

12. DESCRIPTORS

Vitamin A Deficiency, LDCs, Blindness, Economic, Social, Nutrition, WHO, FAO

13. PROJECT NUMBER

14. CONTRACT NUMBER

AID/TA/N

15. TYPE OF DOCUMENT

Status Report

AID 590-1 (4-74)

VITAMIN A, XEROPHTHALMIA, AND BLINDNESS
A Status Report in Three Volumes

Volume II

VITAMIN A
PROBLEMS WITH SPECIAL REFERENCE TO LESS DEVELOPED COUNTRIES

by
Andre G. van Veen, Ph.D.
and
Marjorie Scott van Veen, M.Sc.

July 1973

Office of Nutrition
Technical Assistance Bureau
Agency for International Development
U.S. Department of State

P R E F A C E

There is a general consensus among those working on the problem that a coordinated effort by the several concerned international donor organizations could sharply reduce the incidence of Vitamin A deficiency caused blindness.

As one of the concerned Agencies, the U. S. Agency for International Development (A.I.D.) has sponsored the preparation for its own use and for distribution to scientists and institutions engaged in Vitamin A programming a comprehensive review of the "state of the art" with respect to Vitamin A requirements, deficiencies, diagnostic criteria, ongoing programs and available technology.

Dr. Jack Bauernfiend, Dr. Wadie Kamel, Dr. Andre G. van Veen and Ms. Marjorie Scott van Veen have prepared three volumes covering Vitamin A, technology, problems and programs. Each volume is an independent effort. Titles and authors include:

A Global Survey of Mass Vitamin A Programs - W. W. Kamel

Vitamin A Problems with Special Reference to Less Developed Countries - Dr. A. G. van Veen and Ms. van Veen

Vitamin A Technology - J. C. Bauernfeind

Each volume is an expression of the author's own style, insights, and experiences focused on the area of his particular expertise. Of necessity, there is some overlap in material but such information is complementary rather than redundant.

This compilation should be considered a first step in an improved and expanded inter-agency program to combat Vitamin A deficiency worldwide. This comprehensive review can serve as a guide to A.I.D. and others interested in Vitamin A programming.

We are grateful to the authors and to Hoffman La Roche, Inc. and to the University of Illinois Medical Center for making it possible for Dr. Bauernfeind and Dr. Kamel to complete these assignments.

Dr. Martin J. Forman, Director
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I. INTRODUCTION

Vitamin A deficiency is known to be a problem of major public health significance in a number of less developed countries. In its acute form in young children it leads to partial or total blindness and thus has widespread economic and social implications. Not enough is known about the extent and seriousness of less acute forms of hypovitaminosis A. The problem as a whole is commanding increasing interest and attention.

This "position paper" is a contribution to CDC-AID efforts to delineate the problems and the possibilities for concrete assistance. In the course of preparing the report, discussions were held with FAO nutrition staff in Rome, and WHO nutrition staff in Geneva.

II. TERMINOLOGY

In view of the complexity of the vitamin A problem, and the confusion that can easily arise in any consideration of it, it seems useful at the outset to define some of the terms that will appear frequently in the report. (1, 2)

Vitamin A: This is a generic term, applied to all compounds having vitamin A activity. It includes the preformed vitamin A (vitamin A_1 alcohol) chemically known as retinol, found in food sources of animal origin such as milk fat, egg yolk and liver, and the provitamins A or certain carotenoids which are colored substances found in some foods of vegetable origin such as green leafy vegatables and yellow vegetables and fruits. The body is able to convert certain carotenoids into the active vitamin. Of the carotenoids, B carotene has the highest vitamin A activity; the vitamin A activity of other carotenoids varies and may be taken to be about 50% that of B carotene. As shown in Chapter III of this report, a number of factors may adversely influence the body's ability to absorb and utilize the provitamins.

Measurement: The custom of expressing vitamin A activity in terms of International Units (I.U.) is slowly giving way to expressing it in terms of micrograms (ug) of retinol. One I.U. of vitamin A is equivalent to 0.3 ug retinol, or in the case of the provitamins to 0.6 ug B carotene and 1.2 ug other total mixed carotenoids. In evaluating foods or diets, account must be taken of the fact that the provitamins are not used by the human body as efficiently as retinol. In the light of present know-

ledge on utilization efficiency, total vitamin A value, sometimes referred to as retinol equivalence, may be calculated as the sum of:

ug retinol

ug B carotene x 1/6

ug pro-vitamin A carotenoids other than B carotene x 1/12

When the estimated distribution of vitamin A activity between B carotene and other carotenoids in a mixture is not well established, the micrograms of the mixture should be multiplied by 1/9, as an estimate of its retinol equivalence.

Vitamin A Deficiency: (Hypovitaminosis A): The presence of depleted tissue stores and low blood levels of vitamin A resulting from a prolonged deficient dietary intake of the vitamin that may be complicated by other factors (i.e. certain diseases), and leading inter alia to serious clinical lesions of the eye.

Hypervitaminosis A: This report is concerned essentially with hypovitaminosis A, but the dangers of hypervitaminosis must be recognized in undertaking programs to eradicate hypovitaminosis A. Excessive intake of the preformed vitamin may have immediate and acute toxic effects; symptoms of excessive intake include anorexia, hyperirritability, skin lesions, bone decalcification and increased intracranial pressure. Little is yet known about the effects of chronic hypervitaminosis A. Carotenoids in massive doses are not converted into vitamin A rapidly enough to induce toxicity; the excess carotenoids accumulate in the body without producing clinical symptoms other than yellow skin. This quickly returns to normal when carotenoid ingestion is stopped.

III. REQUIREMENTS FOR VITAMIN A

Background

Knowledge of human requirements for nutrients is essential in planning food production and supply programs, in assessing food consumption levels and in guiding public health nutrition programs. The establishment of requirements for vitamin A poses many problems. The functions of the vitamin in the body have not yet been fully elucidated. Its role in vision is best understood. It does not appear to function in metabolic systems related to energy production. Therefore, the practice has been maintained of expressing requirements "per age group" or "per kilogram of body weight". The metabolism of vitamin A is still poorly understood. Under normal conditions the vitamin is not excreted in the urine and there is little information on the urinary excretion of its metabolites. The vitamin accumulates in the body and is stored mainly in the liver, thus, the criteria of adequacy are limited to clinical lesions, mainly of the eye, and levels of the vitamin in body fluids and tissues (i.e. blood and liver). There is much evidence derived from animal experiments that the relationship between serum levels of vitamin A and liver reserves is not simple. However, it would appear that in an apparently healthy individual, low serum level of the vitamin is indicative of a poor liver store and a prolonged low intake of the vitamin.

In general, two types of data have been used to estimate human requirements for vitamin A. Firstly, there are field studies on human population groups in which attempts have been made to correlate clinical

evidence of vitamin A deficiency and/or levels of the vitamin in the blood with dietary intake of the vitamin. Such studies have shown that clinical evidence of vitamin A deficiency seldom occurs in individuals consuming 3000 - 9000 I.U. per day, but may occur when the daily intake is of the order of 1000 - 2500 I.U. 1/(1)

The second type of data is from controlled depletion studies, both on man and on animals of various species, in which clinical manifestations and/or changes in blood vitamin A levels developed on a certain dietary intake of the vitamin are abolished by specified increases in intake of the vitamin. The so-called Sheffield Experiment carried out on healthy male volunteers between 20 and 30 years of age in 1942 is still considered the best controlled of the human depletion and recovery studies, albeit recovery was studied in only three subjects. It was concluded from that study that 390 ug retinal (about 6 ug per kg body weight) per day were needed to restore defective dark adaptation and rod scotometry patterns to those found in well-nourished individuals. However, the 390 ug dose level of retinol was not sufficient to restore the blood vitamin A level to that found before the depletion period; this was achieved when intake was increased to 750 ug retinol per day.

In the case of infants, children and adolescents, there is no direct evidence from which requirements for vitamin A can be estimated. It has

1/ The original surveys do not supply data relating to the actual intake of retinol and carotenoids, hence the international unit is used.

become necessary to base such estimates on epidemiological and other circumstantial evidence. Difficulties inherent in the conduct of metabolic studies in children and possibly ethical considerations that may limit undertaking such studies are largely responsible for lack of precise knowledge of requirements of this important and vulnerable sector of the population. In the words of one authority on vitamin A, "Our ignorance about the nutrient requirements of children and adolescents is to say the least abysmal." (3)

Current Requirement Figures

The most recent consideration of requirements for vitamin A has been given by an FAO/WHO Expert Group on Requirements of Vitamin A, Thiamine, Riboflavin and Niacin in 1965 and by the Food and Nutrition Board of the National Research Council (USA) in 1968. (1, 4)

Commonly used terms in the literature such as "minimum requirements," "optimum requirements" and "recommended allowances" unless well-defined tend to promote confusion, having different meanings for different people. The FAO/WHO Expert Group adopted the following definition:

> "Recommended Intakes: The recommended intakes for vitamin A, thiamine, riboflavin and niacin are the amounts considered sufficient for the maintenance of health in nearly all people."

The Expert Group's recommended intakes of retinol for different age groups based on its consideration of available data, are given in Table 1. On a body weight basis they vary from 65 ug per kg at four months of age to 12 ug per kg for the adult as shown in Figure 1.

It is not uncommon for the very important footnote to Table 1 to be overlooked. Adjustments in the figure for retinol must be made when diets contain both retinol and carotenoids, as indeed is generally the case. The procedure for doing so is described later in this chapter and the recommended intakes of the vitamin in relation to the proportion of B carotene in the diet are given in Table 2.

The Expert Group emphasized that "the recommended intakes are not expected to cover any additional needs for these vitamins which may result from abnormal conditions such as microbial and parasitic infections, malabsorption syndromes or metabolic abnormalities of genetic or degenerative origin. Nor are they intended to be sufficiently high to meet the requirements under extreme environmental conditions. Furthermore, these recommendations are applicable only when the requirements for calories and all other nutrients are fully met". It will be obvious that the recommendations are not applicable in less developed countries (LDCs) where dietary intake, quite apart from vitamin A, is often suboptimal and where infectious diseases are so common.

The Food and Nutrition Board maintained its custom of expressing vitamin A in terms of International Units, and its recommended allowances for different age groups are given in Table 3. In the opinion of the Board, its recommended allowances will "maintain good nutrition in practically all healthy persons in the United States". With the exception of calories, they provide "a buffer against increased needs during common stresses and permit full realization of growth and productive potential,

but they are not necessarily adequate to meet the additional requirements of persons depleted by disease, traumatic stresses, or prior dietary inadequacies. However, the allowances are generous with respect to temporary emergency feeding of large groups under conditions of limited food supply and physical disaster". Thus, these recommendations also are not applicable to conditions generally prevailing in LDCs.

If the two sets of recommendations are reduced to a common denominator (i.e., retinol equivalence) taking into account that it is estimated that 50% of the vitamin A in the U.S. dietary pattern is in the form of the provitamin, it will be found that the differences are slight for most age groups; for infants and for lactation, the FAO/WHO figures are higher. (Table 4)

Two differences between the two sets of recommendations may be noted. The FAO/WHO Expert Group did not recommend an increase above the normal adult level during pregnancy, assuming that the habitual diet of the woman provides 750 ug of retinol per day (i.e. that she is well nourished and has "normal" liver reserves of the vitamin). This, of course, would not pertain in chronically malnourished populations.

The FAO/WHO Expert Group's recommendations do not include a figure for infants under 6 months of age, it being accepted that breast feeding by a well-nourished mother is the best way to satisfy the nutritional requirement of the infant for vitamin A. In many areas, of course, mothers will themselves not be well-nourished and furthermore breast feeding may be

replaced by the more prestigious artificial method to the great detriment of the infant if suitable weaning foods or food preparations are not available and used (see section on protein-rich foods in Chapter VII). Decline in breast feeding is a modern trend in most all countries, and particularly in urbanizing areas.

A Technical Group convened by the Pan American Health Organization in 1969 to consider hypovitaminosis A problems in Latin America endorsed the use in Latin America of the vitamin A recommendations of the FAO/WHO Expert Group. (2) It is understood that a number of countries in other areas have likewise adopted them.

Factors Influencing Vitamin A Requirements

Neither physical activity nor climate per se appear to influence human requirements for vitamin A. On the other hand, a number of infectious diseases commonly found among children and adults in the LDCs are known to play an important role in precipitating a vitamin A deficiency, or in aggravating an existing one (i.e. diarrheas, measles, chicken pox, whooping cough, malaria, ascaris, hookworm, tuberculosis) because they adversely influence the absorption, transport and utilization of the vitamin. The effects are likely to be greater in the case of the provitamins such as B carotene, which is usually the major source of vitamin A in these countries, than with retinol itself. Some dietary fat is needed, especially for the intestinal absorption of the provitamins. Protein is essential for transport of the vitamin in the blood and this may explain in part the close association between protein-calorie malnutrition (PCM)

and vitamin A deficiency that has so frequently been reported. For example, in Indonesia such association may be found in about 75% of the cases of PCM; on the other hand, in countries of the Near East less than 10% of such individuals may simultaneously suffer from overt vitamin A deficiency.(5) Such differences may reflect differences in eating patterns and perhaps in disease patterns. Antibiotics and other drugs, including laxatives, may decrease absorption of the vitamin from the intestinal tract.

Application of Current Recommendations

The approach of the FAO/WHO Expert Group to vitamin A requirements is scientific and innovative and probably heralds a methodology that will be widely used in the future. At the present time its practical application involves a number of difficulties, some more difficult to deal with than others. These are distinct from the fact that few food composition tables express vitamin A activity as retinol and B carotene.[1/]

Intake figures recommended by the FAO/WHO Expert Group are expressed as retinol. But diets generally contain retinol and provitamins (some carotenoids) in varying proportions. In the LDCs the proportion of

1/With respect to regional tables, "The INCAP-ICNND Food Composition Table for Use in Latin America (1961)" gives the "vitamin A value" in micrograms retinol. "The Food Composition Table for Use in Africa (FAO-U.S. Dept. of Health, Education and Welfare, Public Health Service, 1968)" gives data on retinol content and B carotene equivalent, both in micrograms. The latter figure can be converted into retinol by multiplying by 0.167. The same method is used in "Food Composition Tables for Use in East Asia" prepared by U.S. Dept. Health, Education and Welfare, CDC and FAO which is currently in press. "Food Composition Tables for Use in the Middle East - American University of Beirut, 1963" give vitamin A value in International Units.

provitamins may be as high as 90% or higher. Furthermore, the provitamin component of the diet is used much less efficiently than retinol itself. The few data available indicate that the absorption of the provitamin from various dietary sources varies considerably; this holds even for B carotene which, in general, is better absorbed than the other carotenoids. The fiber content of foods is known to influence absorption. For example, B carotene is absorbed to a greater extent from papaya than from carrots; it is better absorbed from carrot puree than from raw carrots because of the influence of cell rupture. Only a limited range of foods has been so studied. The B carotene content of leafy vegetables is subject to variations of 10 - 20 fold and depends on the maturity of the plant and the part of the plant sampled. (6)

Pending more experimental evidence on absorption and utilization of the carotenoids, the recommendations of the FAO/WHO Expert Group are relevant, namely that the utilization of B carotene is about 1/6 that of retinol, and the utilization of other provitamins is about 1/2 that of B carotene. Thus, while retinol has full biological activity, 1 ug B carotene is equivalent in biological value to only 0.167 ug retinol.

The conversion of recommended intake figures for retinol into intake figures of mixed vitamin A active compounds, that accounts for the proportion of vitamin A active carotenoids in a given dietary pattern and their biological value, involves some mathematical niceties that can be condensed into the following formula:

$$\text{Recommended intake of mixed vitamin A active compounds} = \frac{\text{Recommended intake of retinol}}{0.167\,k + (1 - k)}$$

where K = proportion of B carotene in the diet[1/]

$$= \frac{\text{B carotene (ug)}}{\text{B carotene (ug)} + \text{retinol (ug)}}$$

Conversely, if an adult has been found to be consuming, for example, 250 ug of retinol and 2400 ug of B carotene, this would be equivalent to a total retinol intake of $250 + \frac{2400}{6} = 650$ ug. This can be compared to the recommended intake for an adult of 750 ug retinol.

Thus, the FAO/WHO Expert Group methodology provides for account to be taken of the proportion of vitamin A activity of the diet provided by carotenoids, which as emphasized may vary very considerably. Table 2 gives the recommended intakes of vitamin A (ug) at various ages in relation to the proportion of B carotene in the diet. On the other hand, the NRC recommended allowances are based on the assumption that 50% of the vitamin A activity in the U.S. diet is from carotene, and no methodology is suggested for adapting the allowances to other patterns of vitamin A intake.

In summary, estimates of human requirements for vitamin A have been reached on the basis of very scanty evidence. The recommendations of the FAO/WHO Expert Group have an advantage over those of the NRC in that they may be adapted to diets containing varying proportions of carotene. It would seem from the considerations put forward in this chapter that in

1/It is assumed that other naturally occurring vitamin A active carotenoids will be included quantitatively on the basis that they have one-half of the biological value of B carotene.

countries or areas where vitamin A deficiencies and other forms of malnutrition, especially PCM, are prevalent, where foods provide the vitamin largely in the form of carotenoids and where infectious diseases are common, the requirement figures for vitamin A recommended by the FAO/WHO Expert Group and by the Food and Nutrition Board of the National Research Council should, at best, be considered minimal targets for improving food production and consumption. Their application in any one country must take account of a number of indigenous factors characteristic of such, apart from vitamin A food sources per se.

IV. GEOGRAPHICAL DISTRIBUTION OF VITAMIN A DEFICIENCIES

Anyone who tries to obtain a realistic picture of vitamin A problems in different countries or areas will end up with a feeling of disillusionment after having read the extensive documentation on the subject. The clinical manifestations of vitamin A deficiency have received considerable attention, but with few exceptions broad-based epidemiological evaluations of vitamin A nutriture have not been carried out in the LDCs. From hospital records, dietary surveys (for the most part done on a small scale and without account being taken of seasonal variations) and limited number of biochemical determinations in blood one cannot extrapolate to large populations. Food supply data give some information. Reliable and truly informative health statistics relating to the problem seldom exist. Available information is scarcely ever comparable from country to country with respect to year, or to season. At best, one can draw only some sketchy conclusions.

The results of ICNND nutrition surveys carried out in a number of LDCs in different parts of the world, using comparable techniques, have provided valuable information on diets, biochemical parameters and clinical evidence of various nutritional deficiences. The surveys have varied with respect to proportion of population covered, and they were carried out over a period of many years. With respect to vitamin A, the surveys have provided some evidence of dietary and biochemical deficiencies of vitamin A, but given little indication of the prevalence of xerophthalmia. Severe xerophthalmia is not likely to be found in the course of such surveys since

it usually occurs in very malnourished children who are apt to have died or to be in the hospital. The comprehenisve ICNND surveys carried out in Central America 1964 - 1967 provide more extensive information on vitamin A problems. (2, 7)

Some clues to the geographical distribution of vitamin A deficiency can be gained from available clinical evidence and data on food supply and consumption.

Clinical evidence:

While skin abnormalities may occur in vitamin A deficiency, they are not specific. Abnormalities in the eye are the only reliable signs for diagnosing clinical evidence of vitamin A deficiency in man. These include xerosis, night blindness, Bitot spots, xerophthalmia and finally keratomalacia. Xerosis and Bitot spots are less specific; night blindness may be due to non-nutritional causes, and moreover is most difficult to diagnose in young children. Thus, xerophthalmia and keratomalacia remain the most trustworthy indicators of vitamin A deficiency. Unfortunately, they represent a very late and very acute stage of vitamin A deficiency and prompt treatment is essential to prevent partial or total blindness. It is becoming customary to use the term "xerophthalmia" to cover the whole clinical syndrome of vitamin A deficiency as it pertains to the eye. The available literature is, however, not always consistent in this regard and this causes confusion in interpreting data.

In an environment where xerophthalmia is endemic, infants, toddlers, school children and adults may suffer, but the affection rate differs widely. The toddler group 2 - 5 years of age is preeminently affected, the peak incidence being in the 3rd and 4th year. Table 5 illustrates this.

The epidemiology appears analogous to that of PCM. Outbreaks of xerophthalmia often correspond directly with seasonal diarrheas and infections of childhood such as measles. (8)

Xerophthalmia has long been known to be endemic in some countries of South and East Asia, such as Indonesia and South India, and has been extensively documented. In many other LDCs, the condition has often been reported, but less thoroughly investigated. In some parts of Africa, especially West Africa, where red palm oil is a common article of diet, xerophthalmia seldom occurs.

The survey of Oomen, McLaren and Escapini made in 1962-63 at the request of WHO in an effort to elucidate the significance of the problem in the LDCs is especially noteworthy. (9) The countries covered were in South and East Asia, Middle East and North Africa and in Central and South America. Data were obtained from questionnaires to governments, hospital records and personal observations.

In considering the findings, it must be borne in mind that government statistics seldom, if ever, record vitamin A deficiency, and to do so would in fact be most difficult because of the common association of vitamin A deficiencies with other diseases, both nutritional (i.e. PCM) and infectious, and because outbreaks of acute vitamin A deficiency are often seasonal. Census figures can be useful in pinpointing causes of blindness if the age at which the condition began is accurately noted. For example, when blindness starts in the 3rd or 4th year, xerophthalmia is

usually implicated. Many data on xerophthalmia were derived from hospital records, and thus reflect the situation in a relatively small segment of the population; extrapolations to the population as a whole are risky. Personal observations of the consultants were considerably influenced by the limited time available, most of which had to be spent in large centers. It is significant to note that rarely did the consultants encounter a pediatrician, opthalmologist or general physician who had made a special study of xerophthalmia; this has important implications for medical education and training programs.

The survey pinpoints the fact that severe vitamin A deficiency exists in a very large number of LDCs, but it does not enable one to compare the magnitude and the seriousness of the problem from country to country. In general, it would appear that the problem is more widespread and serious in the rice-eating countries of Asia. In Latin America, xerophthalmia seldom seemed to be such a common fellow-traveler of malnutrition as in countries in South and East Asia. In any environment suffering from the bad effects of urbanization, it was not difficult to discover cases.

Experience in Hong Kong exemplifies the role that medical services can play. In this area of extreme population density, xerophthalmia is now a disease primarily of recent immigrants. This is attributed to the fact that since 1953 all young children receive free opthalmic treatment and all children with eye disease of any kind are given a massive dose of vitamin A as a routine part of any treatment. While Japan is no longer an LDC, its experience is noteworthy; the virtual disappearance of xerophthalmia

in recent years is attributed to growing prosperity and increasing "nutrition mindness" of the population. (See chapter VII)

The very considerable recession of xerophthalmia noted in Singapore since 1955 has been attributed, inter alia, to health education, legislation to make addition of vitamin A to all forms of processed milk compulsory, availability of maternal and child welfare clinics and improvement in economic standards. (10)

At the end of 1963 WHO began an epidemiological study in Jordan which included a field investigation and a study of patients admitted to hospitals for xerophthalmia. The survey covered 1180 children under 6 years of age. A prevalence of 8% of mild to moderate xerophthalmia was found among these children, with a peak incidence between 30 and 40 months of age, probably indicating that the infants were born with low vitamin A reserves. (11)

In a survey carried out by Escapini in Latin America and the Caribbean in which 2532 children were examined in 11 countries, 14.7% revealed evidences of malnutrition while 1.4% had eye lesions manifested as ulcers of keratomalacia. Xerophthalmia in the malnourished group alone was 9.7% as compared to 1.4% in the total group. The incidence of xerophthalmia was greatest from July to December and corresponded directly to seasonal gastro-intestinal infections of childhood. (2)

A recent survey in Mexico revealed that night blindness, 1 - 2 cases per community, could be found in the north; in the tropical areas of the south of Mexico there was xerophthalmia both with and without other signs of malnutrition. (12)

Food supply and consumption:

A very broad general assessment of some nutrition problems can usually

be gained from National Food Balance Sheets. As pointed out elsewhere in this report, Food Balance Sheets do not report vitamin A and furthermore statistical data on provitamin A foods are scarce and unreliable. At best, Food Balance Sheets indicate that in the LDCs, generally, per caput supplies of foods of animal origin providing the preformed vitamin are low.

Available dietary survey data from LDCs tend to be spotty with respect to proportion of population, specific age groups and seasons covered to permit valid extrapolations regarding the vitamin A problem to the country or area concerned. With few exceptions dietary survey data are reported on a family or average per caput basis and therefore do not reveal the intakes of the specific age groups known to be most susceptible to vitamin A deficiency and for whom intervention programs may be needed. In most cases, carotenoids provide from 60 to nearly 100% of total vitamin A intake, and moreover, the average per caput intake of total vitamin A is usually marginal, or below estimated requirements.

Clinical evidence of vitamin A deficiency seldom occurs in individuals consuming 3000 - 9000 I.U. per day, but may occur when the daily intake is of the order of 1000- 2500 I.U. Data from dietary surveys conducted mainly since 1955 and reviewed by the FAO/WHO Expert Group at its meeting in 1965 indicated daily per caput vitamin A intakes of the order of 1500 - 3000 I.U. in Latin America, 1000 - 2500 I.U. in Asia and the Far East, 500 - 2000 I.U. in the Near East, and 1500 - 4000 I.U. in Africa. It was not possible to express these intakes in terms of retinol or B carotene since in most cases insufficient information was supplied about the sources of vitamin A.

More recent studies confirm deficient vitamin A intakes among families in Central America; a study of 202 pre-school children in rural and semi-rural areas of four Central American countries showed that vitamin A intakes were only about 40% of estimated needs. (2)

In summary, the WHO survey conducted in 1962-63 confirmed the suspicion that xerophthalmia exists as a public health problem in many more countries than was until that time realized, but it provided little, if any, factual information on prevalence. The same applies to more recent studies, and also with few exceptions to the data on biochemical determinations and food supply and consumption. However, all types of data - clinical, biochemical and dietary - are consistent in pointing to serious vitamin A problems in a large number of LDCs.

Discussions held in the course of preparing this report emphasize that widespread vitamin A deficiency in severe form is found mainly in the rice-eating countries of Asia, in particular, Indonesia, South India and Bangladesh. There is growing awareness of the existence of vitamin A problems in the Philippines and some investigations are underway. Although vitamin A problems would appear to be less serious in Thailand than in some other countries of the region, there is interest in them and a well-controlled pilot study has been initiated in Chengmai. In Malaysia vitamin A deficiency problems appear to be localized in some areas in the eastern section. Little is known about the current situation in Ceylon where vitamin A deficiency has long been considered to be an important

public health problem. It would seem likely that vitamin A deficiency is serious today throughout Viet Nam.

In other areas, moderate cases of vitamin A deficiency may be fairly prevalent, but in general, present a less acute problem than in countries in Southeast Asia. This holds, for example, for parts of Africa, especially East Africa. In the Latin America region, vitamin A deficiency in moderate, rather than acute, form seems to be important in El Salvador, N.E. Brazil, N. Chile as well as in Haiti.

The very existence of xerophthalmia in any given population suggests that subclinical forms of vitamin A deficiency may be widespread. The population "at risk" may be many times greater than the population evidencing xerophthalmia. If a population is "at risk" with respect to vitamin A, then stress factors, such as infectious diseases or seasonal food shortages, assume special significance. Simple, practical means that could be used routinely to detect the "at risk" groups of a population would be of great value.

In most countries or areas, broad-based epidemiological or ecological studies are needed to define the nature and the magnitude of the problem of vitamin A deficiency and the proportion of the population "at risk"; such information is essential for planning intervention programs that will be of practical value.

V. DIETARY BACKGROUND OF VITAMIN A DEFICIENCIES

The general pattern of diet in the LDCs is well known. A staple food (cereal or root or tuber) makes up the major portion of the diet. In areas where the staple is yellow maize or yellow sweet potato, these foods may provide considerable amounts of provitamin A. For example, the vitamin A activity of yellow maize may be as high as 450 I.U. per 100 g (13); for some populations, maize provides up to 75% of the total calories and contributes a substantial amount of the vitamin if the grain is eaten whole. Other foods are eaten in varying amounts. With few exceptions, animal protein foods, including milk which is so valuable in the diet of the weaned infant and young child, are notoriously scarce; thus, preformed vitamin A is scarce. Information of this nature is readily available from National Food Balance Sheets. However, the latter, because of statistical and other problems, give little, if any, information on fruits and vegetables, some of which are the chief providers of provitamin A. In arid zones their production is very limited and very seasonal so that both rural and urban zones are affected by a scarcity of the provitamin. In the green tropics, provitamin A sources vary according to the seasons and to food habits. Furthermore, production of fruits and vegetables in LDCs is often limited by traditional cultivation patterns and carried out on a family or other small-scale basis. Supplies may thus, not reach the ever-growing urban conglomerations, or they may be too expensive for the average urban family to buy. Under such circumstances, consumption of the provitamin is very limited. On the other hand, there is evidence in some areas that when a good urban market is accessible the

rural producer sells as much as he can to it to the detriment of his own family. This applies, for example, in parts of Central America where the urban family consumes more than twice as many vegetables and fruits as the rural family. It applies also in Bangladesh where vitamin A deficiencies are prevalent. Population pressure is a factor not to be ignored in considering current or potential sources of vitamin A. For example, in a purely agricultural part of Java in 1970 population density was reported to have reached 1.000 per square kilometer.

In describing nutritional deficiency diseases it is common to emphasize the importance of a single dietary factor. While an inadequate intake of vitamin A as the preformed and/or the provitamin has a dominating position in the etiology of hypovitaminosis A, other dietary factors are involved, and as pointed out elsewhere in this report, infectious diseases also play a very important role. Protein is essential for blood transport of the vitamin. Some dietary fat appears useful, if not essential, for the absorption and utilization of the provitamin. Fat consumption tends to be low in the LDCs. In the few areas where red palm oil, the only vegetable oil known to be rich in carotene, is a common and regular article of diet, such as in parts of West Africa, vitamin A deficiencies are virtually unknown.[1/]

It would appear that when acute vitamin A deficiency is endemic, diet is the overriding causative factor. Apart from a low intake of the preformed

1/ Red palm oil is a rich provitamin A source only when it has not been industrially processed.

vitamin and a low and often fluctuating intake of the provitamin A, there are problems with respect to the absorption and utilization of the provitamins as discussed in Chapter III.

In assessing dietary aspects of the vitamin A problem, it is essential to have information on how vitamin A foods are distributed within the family, and food habits, generally. Consumption of provitamin A rich foods, especially by young children, is often seriously restricted by ignorance and prejudice as well as by traditional ways of preparing them that make them unsuitable or unacceptable to young children. In some areas, fruits such as mangoes and papayas, are consumed before they are ripe and when their provitamin A content is still very low. For example, unripe papaya has 15 ug B carotene equivalents, while ripe papaya has 710. Comparable figures for mango are 110 and 1800. (14)

For infants, breast feeding is of unquestionable importance in forestalling vitamin A deficiency. Experience in Orissa Province, India, is illustrative. (15) There two groups of people, the Oriya and the Khonds, live in fairly similar conditions and have a similarly mild deficiency of vitamin A in their diets. Among the Khonds, pregnancy is regulated by traditional practices; postnatal intercourse is forbidden or avoided until the child can walk and pregnancies are, therefore, well-spaced, allowing the breast-fed child a good nutritional start in life. The Oriya have no such custom and intercourse is resumed soon after child-birth; here vitamin A deficiency is a disease of the deposed child who has been deprived too soon of its mother's milk and attention. Even a small quantity,

regularly consumed, of a food containing the preformed vitamin (i.e. breast milk, cow, buffalo or camel milk) may be beneficial. Also relevant are the current efforts to provide suitable processed protein-rich weaning foods in areas where milk and other protein foods suitable for infants and young children are scarce. (See section on protein-rich foods in Chapter VII.)

Appropriate nutrition education programs can help to alleviate the vitamin A problem whether it be concerned with a low production of vitamin A-rich foods, poor food habits, or maldistribution of vitamin A foods within the family conditioned by tradition, prejudice and ignorance.

VI. DIAGNOSIS OF VITAMIN A DEFICIENCY

The criteria for diagnosing any nutritional deficiency may be clinical, biochemical or dietary. In the case of vitamin A, many factors - nutritional, physiological and pathological - can influence vitamin A status and must be taken into account.

Clinical Criteria

Abnormalities in the eye are the only reliable signs for diagnosing clinical vitamin A deficiency in man. Xerophthalmia is the term commonly used to denote the range of ocular changes that may occur, affecting mainly the cornea and conjunctiva. The first stage is xerosis (dryness) which usually starts in the conjunctivae and then spreads over the cornea. Usually night blindness (hemeralopia) sets in; night blindness is not easy to diagnose, especially in young children, and moreover it may be due to non-nutritional causes. Sometimes, but not always, inflammation starts. Dyskeratosis of the epithelium of the cornea and conjunctivae develop. Sometimes, but not always, white, foamy spots (Bitot spots) may be observed as xerosis spreads over the whole cornea which becomes opaque (gelatinous) and necrotic. This stage is known as keratomalacia and it is at this stage that the cornea may perforate, resulting in partial or total blindness; this last stage may develop very rapidly. Sometimes, but not always, the conjunctivae show hyperpigmentation, but this seems to be a rather doubtful criterion. Corneal blindness in one or both eyes acquired at an early age is often proof of a former episode of xerophthalmia. Although xerophthalmia is usually a bilateral condition, asymetry of the lesion is not proof against an etiology of vitamin A deficiency. (8)

Vitamin A therapy applied not too late in the disease process may save the sight, but Bitot spots, for example, may clear up only slowly, or not at all. Therefore, Bitot spots cannot usually be used for diagnostic purposes unless other clinical signs or low blood levels of vitamin A are also found. Diagnosis of conjunctival xerosis is subject to investigator bias.

Not all eye diseases leading to blindness are caused by a deficiency of vitamin A. Trachoma, for example, seldom causes blindness before adolescence. There is also ophthalmia neonatum, starting in the first weeks of life; cataract and glaucoma are found mainly in the elderly. Smallpox may also cause blindness. However, a high percentage of blindness among children under 15 years of age in a given area is usually the result of xerophthalmia. This condition is often diagnosed too late for treatment to be effective; a high percentage go blind and/or die soon after admission. Often it is possible to detect vitamin A deficiency by biochemical analysis of the blood before there are clinical signs and symptoms in the eye, but such determinations are seldom made.

It is not easy to ascertain what percentage of vitamin A deficient children go blind, or partially blind, or die. An example from Indonesia may be illustrative: in one group of 152 young children, 44 became totally blind, 28 became blind in one eye and 35% died. (8) Of course, one has to take into account that many children who have vitamin A deficiency have also another complicating disease, and may die from it, or from a combination of the disease and the vitamin A deficiency.

Reference has been made elsewhere in this report to the fact that a number of infectious diseases may precipitate vitamin A deficiency, and vice-versa. Therefore, one should always be on the lookout for xerophthalmia after epidemics of such diseases in areas where the vitamin A supply is known to be marginal. Deficiency signs, such as xerosis, may appear and disappear after the diarrhea or other infectious disease has disappeared and the provitamin A intake has increased and the body is better able to utilize it. Vitamin A deficiency in adults is more often precipitated by physiological and pathological stresses such as pregnancy or liver disease than by diet alone.

It will be obvious that the clinical diagnosis of vitamin A deficiency is not a simple matter and should be left to suitably trained medical personnel. Efforts are being made to arrive at a standardized nomenclature and criteria for which there is great need.

Age Distribution

When vitamin A deficiency is endemic, infants, pre-school children and also school children suffer most. However, infants do not readily suffer if they are breast-fed and if their mothers have a good reserve of vitamin A. The influence of infectious diseases of all kinds is especially marked in the young age groups. It appears that adults have higher blood vitamin A levels and that their epithelia are less readily affected by vitamin A shortage, although typical clinical signs of vitamin A deficiency may occur in adults.

Mortality

Because vitamin A deficiencies are usually accompanied or precipitated by other diseases and vice versa, it is practically impossible to determine mortality rates in connection with vitamin A itself. Usually, the death of individuals with severe vitamin A deficiency will be recorded, and probably rightly so, as being due to the "other" disease (i.e., PCM or measles). Frequency of blindness in the young and of vitamin A deficiency are usually correlated; frequency of deaths and vitamin A deficiency are not. In most cases, vitamin A deficiency is a contributing factor, but not the main cause of death.

Biochemical Criteria

There are several different biochemical macro and micro methods for estimating vitamin A and carotenes in blood. A number of these are described in the ICNND Manual for Nutrition Surveys which is widesly used. (16) It is generally assumed that levels of retinol are a reflection of dietary intake over a long period of time, rather than of immediate past dietary intake. On the other hand, carotene concentrations are thought to reflect immediate past dietary intake of these pigments.

Measurement of vitamin A in blood is technically more complex than that of many other vitamins. Results tend to vary with the method and apparatus used; hence, results obtained from different laboratories are often not comparable. Small differences in analytical results have proportionately more significance at low levels of vitamin A than at high levels. Thus, caution is needed in interpreting "deficient" and "low" values. There appears to be a need for standardizing methodology, for

which the collaboration of many laboratories would be necessary. It would appear useful to have a "Reference Center" where samples could be sent for checking and methodology compared.

The range of blood vitamin A concentrations in well-nourished individuals is usually between 30 - 50 ug/100 ml with a few values between 20-30 ug. It is generally agreed that 15 ug does not represent severe depletion. Since considerable amounts of vitamin A may be stored in the body, a long period may be required for stores to be depleted and reflected in lower blood concentrations. Night blindness may appear at various levels, sometimes only when the level has decreased to 2-3 ug/100 ml.

Guidelines for interpreting data on vitamin A concentrations in blood in field studies of population groups are set forth in the ICNND Manual. If 15% or more of the sample has blood values below 20 ug retinol/100 ml, or if 5% or more of the sample has values below 10 ug retinol/100 ml then it may be concluded that vitamin A deficiency is present as a public health problem in that population. A population group having plasma retinol values below 10 ug/100 ml should be regarded as a high risk group, unprepared to face adverse conditions such as temporary shortages of foods rich in vitamin A due to seasonal variations, infectious diseases, etc. At retinol levels below 10 ug, low levels of carotenoids are to be expected. Consistently higher levels of carotenoids accompanying low levels of retinol should be further investigated. Because of the marked differences in serum retinol levels between age and sex groups that have been noted in some surveys, subcategories should be tabulated separately. (2)

Dietary Considerations

Food consumption studies alone are of limited value in diagnosing vitamin A deficiencies. Because seasonal differences in vitamin A intake are common, such studies must be carried out on the same population group at different seasons of the year to provide a realistic picture of intake. Determination of plasma levels of vitamin A can help to confirm, or otherwise, dietary inadequacy.

Studies of food habits can provide valuable information with respect to the use of vitamin A rich foods in general, and their distribution among different age groups within the family. Such studies, however, are seldom carried out.

In summary, although vitamin A deficiency is recognizable from the clinical signs, and can be assumed if the dietary intake and plasma levels of the vitamin are low, there is still no simple method of diagnosing the condition specifically or of evaluating the total stores of vitamin A in the body. (17)

VII. INTERVENTION PROGRAMS

In any country or area, a sizeable intervention program is called for only when vitamin A deficiency is known to be widespread. It will be clear from the preceeding chapters that while vitamin A deficiency is prevalent in many LDCs, often in acute form, available data are only suggestive of the extent and seriousness of the problem in the population as a whole. The pattern of diseases (i.e. diarrhea, measles, etc.) that so often precipitate or aggravate an outbreak of clinical vitamin A deficiency is not necessarily the same from year to year, or from country to country. While the major dietary source of vitamin A in the LDCs is provitamin A (certain carotenoids), there are differences among countries as to the actual foods that are the most important contributors of it. Within some countries, seasonal variations in provitamin A-rich foods often account for seasonal variations in outbreaks of clinical vitamin A deficiency. Variations in food habits related to the consumption of provitamin A-rich foods as well as maldistribution of available supplies within the family likewise occur and may be of great significance. There may also be marked differences in food consumption patterns between rural areas dependent solely, or largely, on local production and urban centers where consumption is dependent on a money economy and where socio-economic factors therefore have paramount importance. Moreover, the situation in rural areas will differ according to whether they are situated in arid zones or green tropical zones. For all these reasons, it is unwise to

generalize as to the types of vitamin A intervention programs that would likely be effective.

Any intervention program should be based on the best available information in the area or country of the vitamin A problem and the particular factors influencing it. This does not mean that action should be delayed pending the outcome of special surveys that are likely to be both time-consuming and expensive; it does mean that all sources of relevant information should be mobilized to provide a basis for planning a realistic program, and supplementary data should be obtained wherever needed. In essence, an ecological or epidemiological approach is needed to determine whether some action should be taken, and if so, what form or forms it should take.

In most countries the age group most seriously affected by vitamin A deficiency is the toddler group and priority attention should be given to this age group in any vitamin A intervention program. Other age groups should be included in an intervention program as resources and opportunities permit, mothers, infants and school aged children being given priority.

Means of treating severe cases of clinical vitamin A deficiency are well-known and fall solely within the purview of medical services. In acute cases, keratomalacia and blindness usually develop very rapidly, often within a few days. Thus, immediate action is needed to dose with vitamin A and to treat the disease(s) that usually accompany the acute stage of vitamin A deficiency.

Therapeutic measures are beyond the scope of this report which is concerned with intervention programs designed to reduce the prevalence of

vitamin A deficiency in a given country, or area, and eventually to prevent its occurrence. They may by divided into two categories: (1) measures for a specific target group reached through a specific type of institution or service, and (2) measures that encompass the population as a whole. Some possibilities will be considered below.

PERIODIC MASSIVE DOSAGE OF VITAMIN A

The fact that the liver stores vitamin A and can build up substantial reserves has suggested the possibility of giving the target population periodic massive doses of vitamin A, orally or parenterally. Available data from clinical trials and from animal experiments indicate that oral administration is preferable. Additionally, it avoids risk of infection that so easily accompanies parenteral administration, and circumvents the negative attitude towards injections that parents have in some cultures.

A field study carried out over a four year period in India gives evidence of the efficacy of a massive dosage program in reducing the prevalence of ocular signs (in this case, xerosis and Bitot spots) of vitamin A deficiency in young children. Initially, 2000 children, 1 - 5 years of age, were included in the study and the annual dose was 300,000 I.U. of a fat-soluble preparation. Higher dosage was considered inadvisable because of the risk of acute hypervitaminosis A. Results reported in 1970 at the end of the study are given in Table 6. During the entire period of the study no new cases of keratomalacia were seen. (18)

A point of special significance arising out of the study is that the percentage of children protected from ocular lesions depended on the age at which the massive dose was initiated. While more than 90% of the

children in the 1 - 2 year age group was protected, only about 75% in the 4 - 5 year age group was protected. This observation emphasizes the importance of giving priority attention to children between 1 - 3 years of age in such an intervention program.

Experience gained in the study suggests that it would be preferable to administer two doses of 200,000 I.U. each per annum at six month intervals.[1/] The field study has laid a sound basis for a program of vitamin A prophylaxis in India and seven States have now embarked on it.

Interest in this approach to reducing the vitamin A problem is spreading in this region. At "A Consultation on the Prevention of Xerophthalmia in Southeast Asia" arranged by WHO/SEARO in Hyderabad, India, March 1972, it was concluded that as a short-term measure the periodic massive dosage technique appeared to be the most practical and rapid way of controlling the condition in this region. (17) Following a short-term, small-scale pilot study in Indonesia, plans have been made for a study on Java in which 200,000 children 1 - 4 years of age will be included. A large-scale program is getting underway in Bangladesh, and in the Philippines a plan is being made to initiate a massive dose study on Cebu which will include, inter alia, a study of the merits of timing the dosage with periods when epidemic diseases such as diarrheas and measles are at their peak. Of special interest is a small-scale, well-controlled

1/ There is some recent evidence that only a portion of such a massive dose is actually absorbed. (19)

pilot study in Chengmai, Thailand. It includes pregnant women and new-born infants as well as pre-school children. The findings should be of considerable interest.

A Technical Group Meeting on Hypovitaminosis A in the Americas convened by PAHO in 1969 made suggestions regarding the administration of massive oral doses of water-miscible vitamin A (100,000 I.U.) quarterly for at least two years to young children from the 3rd month of life, and to lactating women immediately after delivery in areas where avitaminosis A is a public health problem. (2) It will be noted that pregnant women were not included. It has been stated that excess vitamin A in the diet of pregnant women may cause teratogenic effects in the off-spring, but convincing evidence of this seems lacking in the literature.

In Brazil a pilot study using water-miscible vitamin A is underway among pre-school children and work is being initiated in El Salvador.

WHO proposes to convene a meeting of "Investigators" during the second half of 1974 at which findings from these massive dose programs would be discussed. This should be of great value in helping to clarify some of the issues about which there are insufficient data, uncertainty or difference of opinion, such as the appropriate size and periodicity of the dose, oil versus water-miscible preparations, age groups that should be included, criteria and methodology for evaluating the effectiveness of the measure.

It is significant to note that the full cooperation of the medical services in a massive dosage program is essential. Massive dosage carries with it the danger of acute toxic reaction in some cases and needs to be done only under the supervision of a medical doctor, public health nurse

or health worker familiar with hypervitaminosis A. This type of intervention program has the added advantage that the target population would be seen periodically by health personnel, thus providing an opportunity for other health problems to be detected.

A primary advantage of a massive dose program is that it provides an immediate and rapid means of reducing the public health significance of the vitamin A problem. Also, it can be undertaken in a relatively small area where other measures, such as food fortification, would not be practical. As will be clear from other chapters of this report, vitamin A deficiency is a many-faceted problem. Those suffering from it need not only vitamin A, but also need to have their dietary intake improved in other respects. Thus, while massive oral dosage programs offer the possibility of bringing about an early and dramatic reduction in the prevalence of xerophthalmia, simultaneous efforts are needed to improve food supplies and to promote sound habits of diet. Admittedly, these are long-range goals, but as stressed by the regional meetings on vitamin A problems in the Americas and in Southeast Asia, they should be pursued.

ENRICHMENT

Enrichment of a food, or food product, with vitamin A would appear to offer a simple solution to the vitamin A problem. This may include enrichment of imported foods and enrichment of foods produced within the country.

Foods imported into LDCs:

Traditionally, vitamin A enrichment has been concerned mainly with

skim milk, especially dried skim milk, and margarine. Since the end of the Second World War dried skim milk has been used extensively in child feeding programs in LDCs, but only within the last few years has a vitamin A enriched product been available. This was achieved only after extensive and time-consuming research.

The standard of enrichment of the U.S. product distributed under the Food for Peace Program, UNICEF and the World Food Program is "not less than 5000 I.U. per 100 g". The U.S. is the only source of vitamin A enriched dried skim milk. There is considerable variation in the daily per caput amount of dried skim milk provided in the distribution programs for mothers and children in different countries. A daily ration of 30 g per beneficiary would provide 1500 I.U. vitamin A. This figure may be compared with the Recommended Daily Allowance (NRC) of 2000 I.U. for a healthy child 1 - 3 years of age and 8000 I.U. for a lactating woman. In terms of retinol, 30 g enriched dried skim milk would provide 450 ug retinol which may be compared with a daily intake recommended by the FAO/WHO Expert Group of 250 ug for the toddler group and 1200 ug for the lactating woman.

There appears to be little, if indeed any, effort to evaluate the effects of distributing vitamin A enriched dried skim milk, or other vitamin A enriched foods such as CSM (Corn soy milk) or WSB (Wheat soy blend), to mothers and/or young children in areas where vitamin A deficiencies are known to be widespread. It may be that some information

is available locally, depending on the interest and initiative of local workers. But it seems regrettable that no provision was made at the outset of such programs to evaluate their effectiveness.

Foods produced in LDCs:

Stemming from the work of FAO/WHO/UNICEF special protein-rich food products based largely on locally available foods are being produced for infants and young children in a number of LDCs. The FAO/WHO/UNICEF Protein Advisory Group at its 18th Meeting in February 1971 adopted a "Guideline Regarding Protein-Rich Mixtures for Use as Weaning Foods". (20) The following extracts from the Guideline are relevant to this disucssion:

"Protein-rich mixtures should be fortified with vitamins and minerals sufficient to satisfy recommended allowances."

Guideline for composition expressed on a dry weight basis specifies for vitamin A "1300 I.U. (as vitamin A palmitate, equivalent to 400 ug retinol) per 100 g."

"The recommended daily intake of the supplement is usually of the order of 100 g dry weight with a protein content of no less than 20%. If the recommended daily intake is less than 100 g the content of protein and other nutrients should be correspondingly higher. These products should not be recommended for infants below six months of age unless they are specifically treated to ensure complete digestibility."

At the present time it is not known to what extent the Guideline for vitamin A is, in fact, being followed. There are now some thirty products in regular production.

A comprehensive review recently made of the use of protein-rich foods for the relief of malnutrition in developing countries concluded that "to date the impact made in individual countries must on balance be considered to be very limited, judging simply on volume of sales.....There are also indications that the lowest income groups for whom these products are primarily intended are not likely to be the principal beneficiaries unless through institutional distribution and that the products have not on the whole penetrated to the rural areas to any extent". (1)

Guidelines for establishing food fortification programs have been amply documented and will not be repeated here.[1/] Rather, attention will be given to some of the factors of special importance in connection with vitamin A enrichment in LDCs.

Although vitamin A is relatively stable to heat, it is sensitive to light and oxidizes readily and these characteristics must be taken into account in considering the feasibility of enriching any locally produced food in the LDCs. Information is needed on the stability of vitamin A in an enriched food, or food product, during transportation and storage conditions prevailing in tropical and semi-tropical countries, as well as on the effects of local food preparation methods on the biological value of the vitamin.

1/ See, for example, Report of the FAO/WHO Expert Committee on Nutrition: Eighth Report, 1970

In considering the enrichment of a food having a prominent place in the national dietary pattern important factors to be considered are:

(1) The extent to which the food enters commercial channels; rural areas may depend almost exclusively on production for home consumption so that an enrichment program would not encompass them.

(2) The extent to which the food is regularly consumed by specific age groups, in particular, the toddler group which as stated previously should have priority attention in a vitamin A intervention program. It is likewise essential to have information on the upper range of intake of the food in all segments of the population in order to ascertain the safe upper limits of fortification because of the dangers inherent in an excessive intake of vitamin A.

A number of common dietary items have been suggested as possible vehicles for vitamin A fortification in LDCs, such as salt, tea, and sugar; considerable exploratory work is underway.

In summary, it would seem that fortification of the foods in the LDCs does not offer an early solution to the vitamin A problems.

SUPPLEMENTARY FEEDING PROGRAMS

Supplementary feeding programs (i.e. for mothers and young children and for school children) offer a possibility for improving the intake of vitamin A on a daily or frequent basis, through a wise choice of foods and/or the administration of a special vitamin A preparation, including cod liver oil or red palm oil.[1/] Despite the importance attached to

1/ In countries where red palm oil is a customary article of diet, vitamin A deficiencies are rare; where it is not acceptable as a food, it must be administered separately from the diet in some special way.

supplementary feeding programs and the efforts made to support them in LDCs under the Food for Peace Program and by the international agencies, results have tended to be disappointing. Whether or not they could be used effectively for vitamin A intervention depends in large measure on local conditions, resources and initiative. One advantage of an institutionalized program is that control is possible, at least in principle, over actual consumption of a food or capsule.

FOOD PRODUCTION

Vitamin A problems have often been the exclusive concern of medical personnel and nutrition workers. Little, if any, concrete attention is given to vitamin A in planning national programs of food production and supply. National Food Balance Sheets which are the basis in most countries for planning food production and supply programs are expressed only in terms of calories, protein and fat. With respect to vitamin A, statistical data on fruits and vegetables which are the major contributors to the vitamin A supply of the diet in LDCs are at best scanty. Nevertheless, agricultural planners and food producers should be alert to the vitamin A situation in their respective country and encouraged to make provision in their plans and programs for increasing the availability of vitamin A rich foods. To this end, special campaigns may be needed.

In rural areas, programs to encourage the production and consumption of nutritious foods through school and community gardens, etc., such as those widely supported by UNICEF and FAO, can be significant and merit encouragement.

In many cultures, vegetables are unpopular, especially among young children. It would appear that greater emphasis could well be placed on such carotene-rich fruits as papaya and mango that are usually very well accepted. Papaya has an added advantage in that supplies are generally available most of the year.

EDUCATION IN NUTRITION

It is sometimes claimed that the vitamin A problem will be solved as economic and educational levels rise, permitting a wider consumption of foods and raising the intake of the preformed vitamin as well as of protein that is essential to the body's utilization of vitamin A in its various forms. The virtual disappearance of xerophthalmia in Japan in recent years lends support to this hypothesis. On the other hand, it must be noted that Japan has had, especially since the Nutritionists Law and the Nutrition Improvement Law were enacted in 1948 and 1952 respectively, an extensive and intensive program of nutrition education that has encompassed all segments of the population.

In the United States the recent 10-State Nutrition Survey demonstrated that economic factors are not the only cause of vitamin A problems. (22) In the LDCs vitamin A deficiencies have sometimes been found to be less common among the poor than among the better-off. (23)

The fact that nightblindness and Bitot spots in young children are often well-known among local populations is evident from the vernacular terms for them frequently found. (9) Parents need to be made aware that they can prevent their children from developing such conditions by feeding them wisely.

There would appear to be an essential role for well-conceived programs of education in nutrition to play in combatting vitamin A deficiencies. Such programs need to be dynamic and adjusted to fluctuations and changes in the ecology of the problem.

CONTROL OF INFECTIOUS DISEASES

No nutritional deficiency is more consistently synergistic with infectious diseases than is vitamin A deficiency. (24) Vigorous efforts should be made in areas of vitamin A deficiency to control infectious diseases through immunization programs, where such are appropriate, through improvements in environmental sanitation and through education programs focused on parents to encourage good hygienic practices in the home, particularly with respect to the feeding and care of young children.

VIII. SUMMARY AND CONCLUSIONS

From data presented in this report it will be obvious that vitamin A deficiency is widespread in the LDCs, often in acute form, but it is not possible to quantitate the problem in any one country. It would seem that vitamin A deficiency is more widespread and serious in the rice-eating countries of Southeast Asia that in the other regions. The age group in which clinical signs of vitamin A deficiency are most frequent is the toddler group. The extent to which an infant is safeguarded against vitamin A deficiency depends in large measure on how well-nourished his mother was during pregnancy and lactation, and the length of breast feeding.

Vitamin A deficiency is a many-faceted problem, quite apart from the fact that the vitamin is not an entity, both preformed vitamin A and provitamin A contributing to the vitamin A value of the diet. The case of xerophthalmia caused by a diet deficient in vitamin A alone is rare. (9) Other dietary factors are important, in particular protein and fat needed for the absorption and utilization of the vitamin. It must be stressed that vitamin A deficiency is only part of the problem of childhood malnutrition and that the best solution is to improve the diet as a whole, rather than to provide only additional vitamin A. The occurrence of xerophthalmia is intimately related to infectious diseases of childhood, especially diarrheas and measles; any program to reduce the incidence of xerophthalmia should aim to reduce exposure to such infections through immunization programs, improvements in environmental sanitation and the care and feeding of young children in the home.

Recommended Dietary Requirements for vitamin A are based on very sketchy evidence, especially for children, and are designed for normal, healthy populations.[1/] In spite of their limitations for use in situations such as prevail in the LDCs, they provide a target to be aimed at in improving food production and supply in the LDCs. The FAO/WHO recommendations have the advantage that they can be adapted to dietary patterns containing varying proportions of the provitamins.

There are difficulties inherent in current methods for the clinical, biochemical and dietary diagnosis of vitamin A deficiency. Although vitamin A deficiency is recognizable from clinical signs, and can be assumed if the dietary intake and plasma levels of the vitamin are low, there is still no simple method of diagnosing the condition specifically or of evaluating the total stores of vitamin A in the body.

In general, vitamin A intake in the LDCs is largely in the form of the provitamins, and this situation is likely to continue, at least for the masses of the population, until such time as agricultural development and economic improvements generally make it possible for food sources of the preformed vitamin to be increased. While there may be need in many areas,

1/In a monograph published in 1972, the authors state, "In spite of the voluminous literature documenting the common occurrence of vitamin A deficiency among pre-school children and repeatedly deploring the widespread occurrence of irreparable eye damage, we found no reports in the literature of controlled experiments on the retinol requirements of children 2 - 18 years of age". (25)

both rural and urban, to increase the availability of carotene-rich fruits and vegetables, there is a very urgent need to overcome maldistribution of food within the family which has been termed "a potent cause of xerophthalmia". (9)

In any country or area an intervention program on any sizeable scale is appropriate when there is proof that a vitamin A problem is widespread in the population and when the causes for it have been delineated. This calls for an ecological or epidemiological approach. In order to ascertain whether the problem is seasonal, what the influence is of infectious diseases, what the problem is in urban centers versus rural areas, it is important for studies to be made at different seasons. In urban areas where food consumption is dependent largely, or solely, on a money economy, it is essential to take account of economic factors that may be of over-riding importance with respect to the etiology of the deficiency, as well as the type of intervention program likely to be effective. In rural areas it is essential to know local patterns of food production and consumption, and to take into account the influence on family food supplies of "cash crops". In all areas information is needed on food habits with respect to available vitamin A rich foods, i.e., whether they are liked or disliked, whether fruits are eaten ripe or unripe, what the distribution is among different age groups within the family, what is the length of breast-feeding and what are the weaning practices. The resulting information should make it clear whether an intervention program is, in fact, needed, and if so what the

merits are of initiating a program likely to have early benefits, such as periodic massive dosage, or of reinforcing longer term programs of economic and agricultural development. In either case, simultaneous attention should be given to education in nutrition and to control of infectious diseases.

Vitamin A enrichment of an indigenous food or food product may contribute to a solution of the deficiency problem if the enriched item is within the purchasing power and consistent with the food habits of the needy groups. With respect to vitamin A enrichment of foods imported into LDCs, it has been recommended that all dried skim milk distributed through international agencies, the Food for Peace Program, etc., be fortified with vitamin A. (2, 9) Up to the present time, the U.S. is the only source of enriched dried skim milk for such programs.

The impact of any intervention program on the vitamin A problem should be carefully studied. The data collected in the course of diagnosing the problem and planning the type of intervention program to be undertaken should provide a sound baseline and set the criteria for evaluation.

In areas where vitamin A deficiency is widespread, routine, periodic plasma retinol determinations would be of value as a means of monitoring the problem and detecting potential xerophthalmia outbreaks before they occur.

In view of the many different aspects of the vitamin A problem, and in view of the different sources of external aid to help solve them, coordination at the country level among different departments of government is needed in defining the problem and in planning and implementing remedial

measures. A National Food and Nutrition Organization would be the appropriate body for dealing with such matters. In some countries, it may be the National Planning Board.

Extensive recommendations for investigations and research into vitamin A problems have been made by several groups.[1/] (1, 2, 9, 17) As pointed out in Chapter VII, the studies being undertaken in connection with periodic massive dosage should shed light on a number of important issues, and the results of the meeting to be convened by WHO in 1974 to discuss the findings should be of great value.

In the context of this report, other fields requiring early attention include the following:

--efforts to arrive at standard nomenclature and criteria for the clinical diagnosis of vitamin A deficiency should be strengthened; the results should be made widely known to medical and para-medical personnel, as well as included in the basic curriculum in training institutions for such personnel.

--the development of apparatus suitable for use in field studies that would measure night blindness objectively should be explored.

--efforts to standardize methodology for measuring plasma vitamin A levels should be strengthened and coordinated.

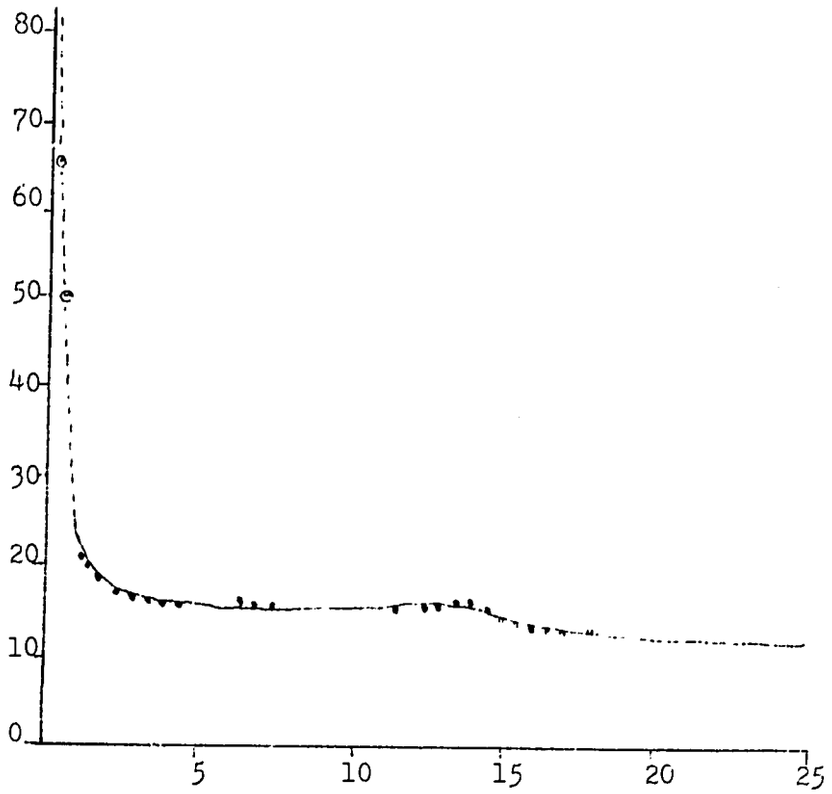
--research is needed on the requirements for vitamin A of the young.

--attention should be given in field studies to the causes for the maldistribution of vitamin A-rich foods within the family.

1/Global Survey on Xerophthalmia; FAO/WHO Expert Group on Requirements of Vitamin A, Thiamine, Riboflavine and Niacin; PAHO Technical Group Meeting on Hypovitaminosis A in the Americas; WHO/SEARO Consultation on Prevention of Xerophthalmia in Southeast Asia.

--agricultural research and extension services should be encouraged to search out and emphasize the carotene-rich fruits and vegetables that can best be produced in their area.

Figure 1. 5. - Basis for Estimation of Recommended Intakes for Children[1]



1/Curve is based on the body weight increment/body weight calculated from reported data (36).

SOURCE: Requirements of Vitamin A, Thiamine, Ribolfavine and Niacin: Report of a Joint FAO/WHO Expert Group, Rome, Italy, September 1965.

Table 1. - Recommended Intake of Retinol at Various Ages

Age	Recommended Intake ug Retinol Per Day	Age	Recommended Intake ug Retinol Per Day
0-6 months	1	10-12 years	575
6-12 months	300	13-15 years (boys-girls)	725
1 year	250	16-19 years (boys-girls)	750
2 years	250	Adults (man-woman)	750
3 years	250	Pregnancy	750
4-6 years	300	Lactation	1200
7-9 years	400		

NOTE: For diets containing both carotene and retinol, adjustment must be made as described on page 25.

1. For infants 0 to 6 months, it is accepted that breast feeding by a well-nourished mother is the best way to satisfy the nutritional requirements for vitamin A.

SOURCE: Requirements of vitamin A, Thiamine, Riboflavine and Niacin: Report of a Joint FAO/WHO Expert Group, Rome, Italy. September 1965.

Table 2. - Recommended Intakes of Vitamin A (ug) at various ages in Relation to the Proportion of B-carotene in the Diet[1]

Age	Percentage of B-carotene in Diet											
	0	40	50	60	65	70	75	80	85	90	95	100
0-6 months	--	--	--	--	--	--	--	--	--	--	--	--
7-12 months	300	450	525	600	650	725	800	900	1 025	1 200	1 450	1 800
1 year, 2 years, 3 years	250	375	425	500	550	600	675	750	850	1 000	1 200	1 500
4-6 years	300	450	525	600	650	725	800	900	1 025	1 200	1 450	1 800
7-9 years	400	600	675	800	875	950	1 075	1 200	1 375	1 600	1 925	2 400
10-12 years	575	850	975	1 150	1 250	1 375	1 530	1 725	1 975	2 300	2 750	3 450
13-15 years	725	1 100	1 250	1 450	1 575	1 750	1 950	2 175	2 500	2 900	3 450	4 250
16-19 years	750	1 125	1 275	1 500	1 650	1 800	2 000	2 250	2 575	3 000	3 600	4 500
Adults	750	1 125	1 275	1 500	1 650	1 800	2 000	2 250	2 575	3 000	3 600	4 500

1/Expressed as $\frac{\text{B-carotene}}{\text{B-carotene + retinol}}$ (ug). Other vitamin A-active carotenoids are expressed in terms on the basis that 2 ug other vitamin A-active carotenoids - 1 ug B-carotene; retinyl esters expressed in terms of their retinol content.

SOURCE: Requirements of Vitamin A, Thiamine, Riboflavine and Niacin: Report of a Joint FAO/WHO Expert Group, Rome, Italy, September 1965

Table 3. - Recommended Daily Dietary Allowances for Vitamin A (NRC)

AGE (years) From		Up To	Vitamin A Activity I.U.
0	-	1	1500
1	-	2	2000
2	-	3	2000
3	-	4	2500
4	-	6	2500
6	-	8	3500
8	-	10	3500
10	-	12	4500
12+			5000
Pregnancy			6000
Lactation			8000

SOURCE: Condensed from "Recommended Daily Dietary Allowances, Revised 1968", Food and Nutrition Board, National Academy of Sciences - National Research Council

Table 4. Comparison of Recommended Daily Dietary Requirements for Vitamin A

NRC - USA			FAO/WHO		
AGE (years) From Up to	I.U.	Retinol Equivalence 1/ ug	Retinol Equivalence 1/ ug	Retinol ug	Age (years)
0 - 1	1500	300	525	300	6-12 months
1 - 2	2000	400	425	250	1
2 - 3	2000	400	425	250	2
3 - 4	2500	500	425	250	3
4 - 6	2500	500	525	300	4-6
6 - 8	3500	700	675	400	7-9
8 - 10	3500	700	975	575	10-12
10 - 12	4500	900	1250	725	13-15
12+	5000	1000	1275	750	16+
Pregnancy	6000	1200	1275	750	Pregnancy
Lactation	8000	1600	2070	1200	Lactation

1/On the basis that 50% of the vitamin A activity is in the form of B-carotene.

Table 5

Percentage Distribution of Xerophthalmia According to Age Groups

Origin[a]	Number	Infants to 1 year	Toddler 1-5	School Age 5-15	Young Adult 15-25	Old Adult 25+
China (1)	203	15.0	17.0	7.0	41.0	20.0
Indonesia (2)	6300	4.4	73.0	13.6	3.8	3.9
India (3)	36	3.0	83.0	8.0	3.0	3.0
Indonesia (4)	890[b]	5.4	88.2	6.4		
Indonesia (5)	166[b]	2.0	80.0	18.0		
Denmark (6)	426[b]	87.0	11.0	1.0		
Japan (7)	1475[b]	2.2	74.8	23.0		
Japan (8)	46[b]	0	76.0	24.0		

[a] Number in parentheses refer to the following sources: (1) Sweet and K'ang, 1935; (2) Oomen, 1957; (3) McLaren, 1956; (4) Oey-Khoen-Liang, 1955; (5) van Wisselingh, personal communication, 1958; (6) Blegvad, 1924; (7) Mori, 1904; (8) Hiro and Yamada, 1936.

[b] Groups of children only.

SOURCE: An outline of Xerophthalmia: H.A.P.C. Oomen International Review of Tropical Medicine, Volume I (1961) 132-213

Table 6
Effect of Massive Dose of Vitamin A on the percent Prevalence of Deficiency Signs

	Incidence in Control Children not Receiving Vitamin A	Incidence in Children who had Received 3 or 4 Annual Massive Doses	Incidence in Children who had Received 1 or 2 Annual Massive Doses
Xerosis	14.9	2.7	6.9
Bitot Spot	9.1	2.6	4.2

All children 5-6 years old at the time of the above analysis

SOURCE: National Institute of Nutrition
Hyderabad - 7: India
Annual Report for the period October 1, 1969 to September 3, 1970
Indian Council of Medical Research 1970

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