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9. ABSTRACT

Effective elimination of vitamin A deficiency in any particular population requires a comprehensive program. This report provides information useful for designing effective, comprehensive programs. It discusses means of assessing vitamin A status, selection of intervention strategies, evaluation of the strategies, research needs in present and future vitamin A programs, and recommendations of the International Vitamin A Consultative Group (IVACG) concerning research and development needs. IVACG recommendations include the following: A permanent Secretariat and information clearinghouse on vitamin A should be set up as soon as possible. So should a reference library. A roster of individuals who are expert in different areas of vitamin A programming should be compiled. Projects should be set up to develop better methods of determining vitamin A precursors, and to standardize methods of collecting and storing tissues in preparation for vitamin A assays. Research should be supported on the physiology of vision, on staining techniques to determine xerosis conjunctivae, on the relationship between vitamin A deficiency and taste impairment and color discrimination, on which foods for various populations are suitable for fortification, and on the absorption, storage, transportation, and excretion of vitamin A supplied by intermittent high-level dosing. Groups or sections within existing institutes or centers should be encouraged to focus specifically on the problem of vitamin A nutrition.

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GUIDELINES FOR THE ERADICATION OF VITAMIN A DEFICIENCY AND XEROPHTHALMIA

A REPORT OF THE
INTERNATIONAL VITAMIN A CONSULTATIVE GROUP
(IVACG)

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Introduction

Effective control or elimination of vitamin A deficiency in any particular population requires a logically formulated series of measures designed with broad understanding of the characteristics of the problem and the population concerned. Assessment, intervention and evaluation are all integral parts of any comprehensive program. However, it is not logical to embark on an assessment of the severity or of the magnitude of the problem without a commitment to intervention if it is found that vitamin A deficiency is a serious problem. Nor is it logical to implement an expensive intervention program without first determining the magnitude, severity, distribution and causes of deficiency. An evaluation of the planned intervention should be built into the program at the outset so that its effectiveness can be analyzed as the program progresses.

The program design, commencing with preliminary assessment and through evaluation of the introduced interventions, should be that judged to offer the most effective approach to the defined goal of correcting the vitamin A deficiency condition. The total program should be managed by skilled personnel and coordinated into the continuing health and nutrition programs within the country.

Special expertise is required at various stages of the program. It is important that talented personnel within the country be developed and utilized to the maximum extent possible and that they be augmented as necessary by external experts (preferably regional) to supplement the required skills. All of the involved personnel and experts should work together as a team under an overall coordinator and with specified assignments and time schedule for accomplishing each step of the program, including reporting on progress and final accomplishment.

This report provides background that it is hoped will be useful in designing effective programs aimed toward eradication for varied situations encountered in regions with avitaminosis A.

I.
ASSESSMENT OF VITAMIN A STATUS
IVACG Task Force on Assessment

Drs. Alfred Sommer, Donald S. McLaren and James A. Olson

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INTRODUCTION

Before any intervention program is launched, a careful assessment of the situation should be made. In general, the sequence of events will be as follows: (a) Government authorities suspect the existence of a serious vitamin A problem; (b) A preliminary investigation is conducted to determine whether formal assessment is justified; (c) A combined clinical and biochemical prevalence survey is instigated to establish:

1. whether vitamin A deficiency exists in the vulnerable age group;
2. the nature, magnitude, severity and geographic distribution of this deficiency;
3. whether this deficiency constitutes a problem of public health magnitude;
4. means of selecting suitable strategies for intervention;
5. a base line for evaluating the effectiveness of future intervention.

A country already planning a general nutritional survey might profitably include within its program the appropriate clinical and biochemical components, without first conducting the preliminary investigation of vitamin A status.

ATTRIBUTES AND ROLE OF THE SPECIALIST

Individuals with specific areas of expertise (managerial, epidemiological, biochemical, statistical or ophthalmological) will be required during different phases of the assessment. At least one specialist, however, should have a wider grasp of the problem. He will be responsible for conducting the preliminary investigation, and, if formal assessment is indicated, should be able to identify which areas require additional support. He will also be responsible for training local field workers in the recognition of clinical signs and for teaching them standard recording procedures.

Furthermore, this specialist should have a broad knowledge of vitamin A, of food and nutrition, clinical competence in the recognition of xerophthalmia, a familiarity with basic epidemiological concepts and expertise in the proper handling of biologic specimens. Experience with the problem in other situations is desirable.

The specialist may be a national or a non-national. The latter may bring the additional advantage of a "fresh look" at the problem with experience gained elsewhere, unbiased by local involvement. He should be tactful in the inquiries that he makes at all levels and should continually bear in mind that the bringing of the whole assessment process to a successful conclusion will depend largely upon his efforts.

PRELIMINARY INVESTIGATIONS

The assessment of vitamin A status and determination of prevalence of xerophthalmia in a community require carefully planned and executed surveys carried out by trained personnel. A preliminary investigation should precede their survey.

The desired information may or may not be available. In order to collate the former and obtain the latter special efforts by a specialist in the field of vitamin A and xerophthalmia are essential.

Collation of Existing Information

Review of the literature: This should be made by the specialist in a center where there is access to the world literature and the usual data retrieval systems. In most instances, this will need to be done before going to the country concerned. A familiarity with the salient geographical, historical, political and socio-economic characteristics of the country is desirable. He should be knowledgeable in the areas of food and nutrition, especially as they relate to vitamin A nutriture and eye disease in the country.

Discussions with individuals familiar with the country: The specialist visiting a country for the first time will find these particularly valuable in helping him to adopt an appropriate approach to his investigation.

Collection of locally available information: Some of this may be obtained from government reports but experience shows that these rarely provide the type of information sought. For example, xerophthalmia rarely can be identified in hospital returns. A general impression of the occurrence of such related conditions as general malnutrition, gastroenteritis and measles can usually be obtained.

Local and regional medical journals, reports of institutes of nutrition and published articles by informed individuals are additional sources of pertinent material.

Records of hospitals, clinics and blind schools should be investigated as the specialist visits different parts of the country. They should be critically evaluated and checked against the impressions he gains through observation and discussion. He should bear in mind that the value of these records is relative to the utilization of these facilities by the population, the competence and interest of local personnel in recognizing and diagnosing xerophthalmia, and the care exercised in keeping these records. It is quite possible for a serious community problem to go undetected at traditional curative facilities.

Obtaining New Information

Interviews with key public health personnel: Many public health workers possess a great deal of information which either has not been recorded or is buried in government files. They can provide an overview of the vitamin A literature, as well as estimates of the incidence of blindness in areas of the country where there are major nutritional problems. If possible, similar discussions should be held with administrative personnel in major regional cities as well as with rural personnel in potential problem areas. All of these public servants have different experiences and perspectives that may provide useful background information.

Contact with directors of schools for the blind, hospitals, pediatric and ophthalmic clinics: Such institutions, although mainly located in major cities, often draw their patients from broad areas of a region or country.

Personal observation and data from blind schools must be evaluated with special care, as only survivors are institutionalized and xerophthalmia carries a high mortality. The eye lesions observable are the sequelae of previous disease, and hence it is difficult to be certain of their etiology.

Structured interviews: This technique consists of preparing a type of questionnaire which is specifically related to vitamin A deficiency, and elicits responses, both verbal and written, from personnel of outpatient clinics, ophthalmological clinics and hospitals in provincial regions. Ideally, a senior investigator should conduct all interviews. In most countries, the personal contact is extremely useful, if not essential, in eliciting a serious response from busy physicians and public health personnel. Information on family expenditure for food, food consumption patterns, infant and young child feeding, and rearing practices might be obtained from health visitors in a similar way.

The careful assessment of hospital records: The assessment of hospital records over a period of years, although a time consuming task, can provide information on age, sex and seasonal incidence of corneal blindness if the records system is designed and maintained in such a way that data on keratomalacia and associated eye problems can be readily and accurately identified.

Questionnaire: Useful information can be gained from properly designed questionnaires which are completed, preferably by interviews with local health personnel in rural communities throughout a country. They should include questions about the community such as: the nature of the major products, activities, educational level, income, food habits, major nutritional deficiencies and the prevalence of infectious disease.

Discussions with village headman: The selected leader of a rural community is generally a capable and respected individual, concerned about the health of young persons in his community. He can often supply information on the incidence of blindness and night blindness, including the time of year when the latter problem is prevalent.

All statistics relating to xerophthalmia should be reported by the specialist in conformity with the WHO classification, following the instructions for its use as given in Appendix I.

PREVALENCE SURVEYS

General Considerations

Regional or countrywide probability surveys are the only unbiased means of determining the frequency (prevalence) and severity of vitamin

A deficiency in the population. These surveys should include both clinical and biochemical determinations whenever possible. A few simple questions, designed to yield *qualitative* dietary intake data may be useful in understanding any deficiency and regional variation observed. Dietary investigations aimed at providing quantitative data may usefully be conducted as part of an intensive follow-up investigation in those areas found to have a significant public health problem, as one of several bases for choosing an appropriate intervention program.

General guidelines for the conduct and analysis of such surveys are provided below.

Preparatory data: Rough estimates of the magnitude and seasonality of the problem will be useful in choosing the sample size and in timing the survey for the period of maximum prevalence. Such data should already be available from the preliminary assessment.

Sample size: In choosing a sample, its size will depend upon two parameters: expected prevalence of the least common clinical criterion and the desired confidence limits. The higher the prevalence, the smaller the sample size required. Expected prevalence can be estimated from existing data, or by employing the suggested criteria for a public health problem (Appendix II). To be meaningful, the prevalence rate should be bracketed by confidence limits. The true prevalence in the population at large has a 95 percent probability of lying within plus or minus two standard deviations of the observed prevalence.

The sampling size should be selected to yield the desired confidence limits. For example, if the corneal scar (XS) rate among 5,000 children is 1 per 1,000 (suggested minimal prevalence for a public health problem), the confidence limits are 0.001 ± 0.0009, a range of 0.1 to 1.9 per 1,000. Increasing the sample size will narrow the confidence limits. By doubling the sample to 10,000 children, the confidence limits are reduced to 0.001 ± 0.0004, a range of 0.6 to 1.4 per 1,000. Since the biochemical criterion for a public health problem is a severely depressed (<10 μg/100 ml) serum vitamin A level in 5% or more of the population, a far higher prevalence than that of corneal scars, only 1 out of every 20 children undergoing clinical examination need to be sampled for a similar degree of precision.

A proper comparison of 2 or more regions requires a complete survey of adequate sample size in each.

Sample sites and season: The sample must be representative of the population under consideration, and the results should be applied to this population only. Hospitals, clinics, schools and day-care centers are not representative of the population at large. The population at risk need not be the entire population of the country or region. One might ignore upper and middle class families, as long as this is noted and weighted accordingly in the result. Since keratomalacia and corneal destruction are primarily afflictions of preschool-age children, surveys should be targeted to this age group (0-6 years old).

Sampling accuracy is improved by stratifying the population into "like" groups (urban vs. rural, desert vs. wet belt), and then choosing sites from within each stratum separately. Field teams must rigorously adhere to the selected sample, and any deviation analyzed for potential bias. The larger the number of clusters (sample sites), the more representative the sample is likely to be.

The survey should be conducted during the season of presumed maximum prevalence of vitamin A deficiency.

Personnel and field activities: Specialists knowledgeable in the clinical diagnosis of xerophthalmia, handling of blood samples and conduct of prevalence surveys should be employed. Every house in a sample site must be visited by a team member, and all eligible children listed and identified. This is the only way to avoid the bias of "volunteer" samples, and to identify the magnitude of potential bias due to absent children.

In clinical surveys, visitation by nurses is desirable, but not necessary. Examination by an ophthalmologist, however, is essential. If more than one ophthalmologist is involved, they must be rigorously and repeatedly standardized against one another. When biochemical analyses are conducted in a local laboratory, a qualified biochemist and adequate facilities for the storage and analysis of samples must be available.

The Clinical Survey

Clinical criteria: Based on the WHO classification of xerophthalmia, the following signs are appropriate for use in the clinical survey:*

(a) Bitot's spots with conjunctival xerosis (X1B). Bitot's spots, in the presence of conjunctival xerosis, are an easily recognized and relatively specific marker of vitamin A deficiency, at least among preschool-age children. They do not provide any information on the prevalence, and cannot be used to estimate the magnitude of ocular destruction and blindness.

(b) Active corneal lesions (X2, X3A, X3B). Corneal xerosis (with or without ulcers) and keratomalacia are the severest forms of vitamin A deficiency. While easily diagnosed and highly specific, their prevalence is usually extremely low.

(c) Inactive corneal lesions (XS). Keratomalacia and corneal xerosis are rapidly destructive, hence rarely encountered in field surveys. It is feasible, however, to assess the prevalence of their sequelae: corneal scars and ocular destruction. It is also important to distinguish between those cases likely the result of vitamin A deficiency, and those due to other causes. This requires a careful examination, preferably with pen light and loups as well as a detailed history from a responsible adult.

Cases of presumed vitamin A related corneal destruction must meet the following criteria: (a) A clinical picture compatible with this diagnosis; (b) The absence of other forms of ocular disease that could have produced a similar picture (advanced trachoma, for example); (c) Historically, the child was at least 4 months old when the lesion first appeared; and (d) The lesions' appearance was unassociated with either trauma, gross purulence or measles.

A history of malnutrition, respiratory infection, or gastroenteritis concommitant with the onset of the lesion is to be expected.

If the history is either vague or unavailable it should be so stated, and these cases reported under different categories: possibly or unlikely the result of xerophthalmia, depending upon the clinical picture. Other causes of corneal destruction should also be tabulated, e.g. congenital, traumatic, infectious, associated with measles.

Although the diagnosis of xerophthalmia-related corneal destruction is retrospective, few if any other conditions produce significant numbers of cases with a similar clinical and historical pattern. Since only survivors are examined, the observed prevalence of sequelae underestimates the incidence of the disease. Photographic documentation of all clinical lesions is useful, wherever possible.

Sample size: The clinical prevalence survey should provide an estimate of the magnitude of vitamin A related corneal destruction. Healed sequelae, the only evidence of such destruction that occurs in sufficient quantities to make such estimates practical, requires a sample size of at least 5,000 to 10,000 children.

Data analysis: To ensure comparative reporting, the xerophthalmia classification should be utilized (Appendix I). When tabulating the frequency (prevalence) of these signs, each child should be included only once, under his or her most severe sign (XS, X3B, X3A, X2, X1B). All such tabulations should be age (in years completed) and sex specific, and include the number positive, the number examined, and the prevalence. The proportion of children with bilateral corneal involvement should be noted. Additional tabulations which may be of interest should be included at the author's discretion.

The Biochemical Survey

Introduction: Plasma vitamin A concentrations of 10 μg per 100 ml or less are closely correlated with inadequate body stores of vitamin A and with clinical manifestations of vitamin A deficiency. Thus, the combined use of both clinical and biochemical data gives a more complete and reliable estimate of the existence of vitamin A deficiency than the gathering of clinical data alone.

In some cases the analysis of vitamin A and total carotenoids in the plasma can be conducted in a local laboratory, but in other instances adequate facilities and personnel are not available for this purpose. In the latter case samples

Other clinical conditions thought to be secondary to vitamin A deficiency are either so subtle, nonspecific, or difficult to measure or standardize that they are unsuitable as criteria for definitive prevalence surveys. These include conjunctival wrinkling, pigmentation, staining with vital dyes, xerophthalmic fundus, night blindness, and perifollicular hyperkeratosis.

might be sent to an International Vitamin A Reference Laboratory for analysis.

Selection, handling and storage of samples: When biochemical analyses are conducted in conjunction with clinical surveys, blood samples will be collected from every 20th child in a random way. In addition, samples will also be collected from every child with clinical signs of active vitamin A deficiency, and a matched control (the next child encountered of the same age and sex who shows no signs of xerophthalmia). Blood samples (0.2 to 0.3 ml) will be drawn by pricking the finger, ear lobe, or heel, collected in non-clotting capillary tubes, and immediately centrifuged. The capillary tube will then be snapped just above the red blood cell-plasma interphase, the open capillary end stoppered with plasticene, and the clear plasma sample labeled and stored under ice in a thermos, or alternatively in a relatively cool place in the dark. Extensively hemolyzed samples should be discarded.

Samples should be transported as soon as possible to a central processing center, where they are immediately analyzed or quickly frozen. The frozen samples may either be analyzed later at the local laboratory or dispatched to the Reference Laboratory. Once frozen, samples should not be allowed to thaw until the time of analysis, since repetitive freezing and thawing is very detrimental. Stored frozen samples should be kept in closed containers in the dark. Unless samples are analyzed within two weeks of collection, the values obtained tend to be unreliable.

Methods of analysis: The major methods for the analytical determination of vitamin A are based on:

(a) the transient blue-colored complexes which retinol and its esters form under anhydrous conditions with a number of Lewis acids (the Carr-Price reaction);

(b) the sensitivity of vitamin A to ultraviolet radiation (the Bessey-Lowry procedure);

(c) the strong yellow-greenish fluorescence at 470 nm which retinol and its esters show when excited at 325 nm;

(d) the spectrum of retinol, which has a maximum absorption peak of 325 nm and an $E^{1\%}_{1cm}$ of 1832 in ethanol; and

(e) The dehydration of retinol to anhydroretinol, which has an absorption maximum of 371 nm and an $E^{1\%}_{1cm}$ ethanol of 3650.

Although all of the above-mentioned methods of analyses for vitamin A are reliable under proper conditions, the recommended procedure for field studies is the micro procedure (0.1 to 0.2 ml plasma) of the Carr-Price reaction, using either trifluoroacetic or trichloroacetic acids (i.e., the Neeld-Pearson or Bayfield procedures). This method has the advantages of simplicity, of widespread use, of single direct reading analysis (as contrasted with difference in readings in the Bessey-Lowry method), of being unaffected by fluorescent contaminants, and of adequate sensitivity. In this assay, as in others, special attention must be given to the proper storage and frequent use of *reliable* standards of crystalline vitamin A.

Although plasma carotenoid concentrations are not indicative of vitamin A status, their analysis together with vitamin A is useful, inasmuch as: (a) high carotenoid levels are associated with the recent ingestion of carotene-containing foods; (b) vitamin A values determined by the Carr-Price reaction must be corrected when carotenoid levels are high; and (c) the analytical procedure for measuring carotenoids is very simple.

Vitamin A in the plasma consists of two major forms, retinol and its ester. Although retinol predominates (> 90%) under most conditions, the retinyl ester concentration may be relatively large under certain conditions. In this survey, separate measurement of these two forms was not considered to be worth the additional expense and time required.

Knowledge of liver stores of vitamin A in children dying of various causes, although useful in assessing the vitamin A status of a sub-group in a population and possibly in determining the effectiveness of a massive dose program, cannot readily be obtained in the conventional prevalence survey. Similarly, measurement of the retinol-binding protein concentration in plasma, although interesting in determining the effects of protein energy malnutrition and other conditions on plasma vitamin A transport, is not of real utility for assessing the prevalence of vitamin A deficiency.

Data analysis: The vitamin A status of the population is assessed by vitamin A values on the random sample of children undergoing clinical examination. Correlation of clinical and biochemical deficiency is accomplished through a comparison of serum vitamin A values in children manifesting clinical disease and their matched controls. In both instances, the median, mean, range and standard deviation of values, the percent <10, μg vitamin A per 100 ml, and the number of samples analyzed should be given. The time between collection and analysis should also be expressed, as well as the manner in which samples were handled and stored. With regard to carotenoid values, the median, mean and range should be given. The method of correcting vitamin A values when carotenoid concentrations are high should be indicated.

USE OF PREVALENCE SURVEY RESULTS

The objectives of conducting a prevalence survey are to indicate the magnitude of vitamin A deficiency as a public health problem and to provide information of use in defining a suitable strategy for reducing its prevalence. The first step is to compare the results of the overall survey with suggested criteria for determining whether vitamin A deficiency is a significant public health problem (Appendix II). On the other hand, administrative leaders in a country may well choose to use their own criteria in assessing the seriousness of the problem and the need for intervention. Whether the prevalence rate is uniform, or whether focal areas of high prevalence exist in certain regions should next be determined. Intervention measures might be limited to a single area of a country or different procedures might be used in different regions.

One or more intensive investigations should be conducted in selected sites of high prevalence in order to better clarify the nature of the target group and the dietary and socio-cultural patterns which favor the development of the deficiency.

Various available strategies for combatting the problem, e.g., massive dosing, fortification, nutrition education, availability of suitable local vegetables and the establishment of garden plots, should then be selected in light of the above findings.

RECOMMENDATIONS

Implementation of the standardized methods of vitamin A assessment outlined in this report requires that the following be established.

1. A pool of international specialists who might be called upon to assist individual assessment projects.
2. A course for training and standardizing international and local specialists in the conduct of preliminary investigation and prevalence surveys.
3. An international vitamin A reference laboratory to support the biochemical component of vitamin A prevalence surveys. This laboratory will process all survey samples when it is not feasible to do so locally. When these are processed locally, the reference laboratory will monitor such determinations by analyzing split samples sent from the field, and forwarding standards to the local laboratory.

APPENDIX I
Xerophthalmia Classification

X1A	Conjunctival xerosis
X1B	Bitot's spot with conjunctival xerosis
X2	Corneal xerosis
X3A	Corneal ulceration with xerosis
X3B	Keratomalacia
XN	Night blindness
XF	Xerophthalmia fundus
XS	Corneal scars
XB	Bitot's spot

Explanatory Notes

1. These signs are descriptive rather than diagnostic. All signs seen at the time of examination are recorded.
2. In general, a progression of severity is reflected in the classifications of signs within the box.
3. The classification can be used both in field surveys and the routine recording of findings in patients in hospitals and clinics.
4. When tabulating the frequency of these signs each child should be included only once, under his or her most severe sign.
5. Only those Bitot spots accompanied by conjunctival xerosis, usually in 0 to 5 year olds, are indicative of vitamin A deficiency. This xerosis may be hidden by the overlying foam of the Bitot spot, and only revealed when this is rubbed away.
6. Secondary signs, located outside the box, often occur in association with, or result from vitamin A deficiency, and should be noted separately.

APPENDIX II
Criteria for Determining Whether Xerophthalmia and Vitamin A Deficiency Is a Significant Public Health Problem

1. X1B $\geq$ 2.0 percent
2. X2 + X3A + X3B $\geq$ 0.01 percent
3. XS $\geq$ 0.1 percent
4. Plasma vitamin A less than 10 μg / 100 ml $\geq$ 5%

Explanatory Notes

1. The proposed tests should be designed and carried out by qualified personnel.
2. These criteria apply only to children 0 to 5 years of age, the population "at risk."
3. The sample of children studied should be representative of the population under consideration. The results apply to this population and this population only.
4. The presence of one or more of the three clinical criteria should be considered as evidence of a significant xerophthalmia problem.
5. The biochemical criterion is strong corroborated evidence of any clinical criteria met. Biochemical data alone are only indicative of significant vitamin A deficiency, and not xerophthalmia.

When the objective is control and prevention of xerophthalmia and its blinding sequelae, these are the parameters which must be measured. When the objective is to improve the general vitamin A nutriture of the population in the absence of significant xerophthalmia, measurement of the milder clinical signs (X1B) and/or biochemical status is sufficient.

II.
SELECTION OF INTERVENTION STRATEGIES
IVACG Task Force on Intervention

Drs. Guillermo Arroyave, J. C. Bauernfeind,
James A. Olson and Barbara A. Underwood

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INTRODUCTION

Before an intervention program can be considered, it is necessary to determine the magnitude of vitamin A deficiency, its causative factors and its geographic location. The assessment of the vitamin A status of a population has been addressed in Part I of this document, but it must be stressed that an intervention strategy rests upon the information obtained from a prior assessment of the problem. It is difficult or impossible to undertake an intervention at the same time as an assessment is taking place. In the same way, the evaluation of a program is dependent upon building into the intervention a mechanism for evaluation at the outset.

Most importantly, a major commitment must exist on the part of the government to solve the problem of vitamin A deficiency. Without this commitment no effective intervention is likely. Many of the intervention strategies require the active cooperation of a number of governmental departments, and thus, a commitment is assumed in selecting the methodology for intervention.

Intervention programs must be viewed in light of the nutrition policy objectives of the country involved. A narrow objective such as the reduction of vitamin A-induced blindness may well call for a different approach than the broader objective of reducing overall vitamin A malnutrition (inadequate intake) in a large segment of the population. Equivalently, the time allowable to reach a particular objective will greatly influence the selection of a strategy. For example, educational approaches or the modification of agricultural production requires a long time to accomplish whereas massive dosing does not. An increase of dietary intake of vitamin A or its precursors by a population from its available resources, coupled with a general improvement in the diet, implies a combination of strategies and requires a long time period for accomplishment.

AVAILABLE STRATEGIES

Massive dosing: refers to the intermittent oral delivery at specific time intervals of vitamin A, in single doses ranging from 100,000 to 300,000 I.U.

Nutrification: (fortification) is a nutrient delivery system involving addition of vitamin A to one or more foods widely consumed by the population.

Horticultural approaches: refer to stimulating the production of fruits and vegatables of high vitamin A activity, at the community or family level (micro), or at the national level (macro), leading to the greater consumption of these by the population at risk.

Nutrition education: is an instructional program conducted through both formal and informal channels, designed to improve food consumption practices as they relate to health concerns and vitamin A nutriture in particular.

Socioeconomic approaches: involve measures to increase the effective demand and utilization of food sources of vitamin A such as improved marketing or a more even income distribution.

Public health: refers to health programs devised to alleviate environmental factors which contribute to the inadequate utilization of the vitamin.

Combined interventions: refer to utilizing more than one of the above to accomplish the goal.

The various strategies are discussed below and their major characteristics are summarized in Table I.

Massive Dosing

This intervention involves a deliverer-recipient individual contact at specified times and therefore a delivery system with a high requirement of personnel, although personnel need not have a high level of technical expertise. There must also be in existence an organized network for contacting the population, preferably under a pre-existing program of the health sector. The cost and responsibility for initiation and continuous implementation of the program usually must be born by the government. This strategy has the advantage of immediate implementation but suffers from the disadvantage that it applies only to the isolated nutrient, vitamin A, and requires repetitive administration. In addition, complete coverage is seldom achieved and members of the group most at risk are often missed, thus decreasing the efficacy of the program. Of the total cost, the major percentage is in the mechanism for delivery and not of the nutrient per se. Furthermore, the program costs continue for the duration of the intervention. Insofar as possible the cost of distribution should be reduced by utilizing pre-existing channels. Monitoring of the program is difficult since efficacy can only be judged at the individual recipient level, either that of the deliverer or the one to whom delivery should occur.

Essentially two levels of risk are involved in this strategy.

1. The dose does not reach all children, particularly the sick child most at risk of irreversible health consequences, because of the nature of the distribution pattern or system.

2. Abuse or misuse of the high potency preparation can produce hypervitaminosis, symptoms which usually are reversible.

Nutrification

This strategy requires the acquisition by survey of food consumption data to determine which foods or food ingredient are more or less uniformly consumed by the population segment involved. Food items can be considered as potential carriers of the added nutrient (vitamin A) if they meet the following criteria: (a) central locations of processing and distribution; (b) a stage of processing which will permit the uniform incorporation of the nutrient; (c) acceptable performance regarding nutrient stability and bioavailability of the nutrient; (d) absence of flavor, taste and textural changes of the nutrified food; (e) availability at a reasonable cost. Personnel skilled in food science and technology are required to initiate the program but once the nutrification process is successfully introduced its control and future monitoring is relatively easy to maintain by limited numbers of personnel in industry and/or government. Some initial costs are involved in the purchase of equipment which will mechanically and uniformly introduce a form of the nutrient into the food product and the necessary laboratory equipment and methodology for assay control of the operation. Thereafter the primary cost of the nutrification strategy is the nutrient or nutrients involved. The cost of nutrification can be borne by government, industry or passed on to the consumer in the purchase of the nutrified product. Implementation of nutrification is relatively simple inasmuch as specific industrial equipment, namely feeders and blenders, have been in existence for some time. Expertise for specific projects exists in the technical service departments of industrial manufacturers of equipment and industrial suppliers of the nutrients, as well as in outside consultants specializing in the field. The monitoring of the nutrient going into the food supply can be easily and continuously carried out at the food factory level. The disappearance of the food supply at the point of consumer distribution is also measurable. Since the added nutrient in the nutrification process goes to the consumer at low daily levels of intake, there is no risk of potential nutrient toxicity. The only area of concern in this strategy would be a drastic shift in food consumption patterns which might occur in times of catastrophies. The assumptions implied in nutrification are: (a) that nutrification changes in a dietary can be made without participation of the consumer; (b) that more than one nutrient can be added at a time; and (c) that nutrient levels can easily be changed, hence the specifics of the nutrification process can be kept updated with current nutritional knowledge on the recipient population segment.

Horticultural Approaches

Two quite different approaches can be taken to horticultural production: by using macro aspects (methods) which deal with agricultural policies, including incentives of developing specific crops, modification of distribution and marketing systems, subsidization of foods for specific target groups in the population and the like; and by using micro aspects (methods) which include initiating family and community projects for growing specific nutritious foods in small garden plots at home and at schools in the community for local consumption.

a. *Macro:* The interrelating of crop production to the nutritional needs of the populace, is an essential ingredient of any serious governmental program in the field of nutrition.

The advantages of such a program are that:

1. government officials thereby demonstrate their commitment to improved nutriture of the populace;

2. a significant shift in the orientation of the agribusiness sector towards improved nutriture will have an important impact on socioeconomic development as well as on nutritional well-being; and

3. the general availability of nutritious, low-cost foods will significantly improve the general nutritional status of the populace, including that of vitamin A, if coordinated with an educational input.

The constraints are that: the costs are high; the program requires active support of many powerful leaders and administrators in a country; and significant visible health changes occur slowly. Key personnel will include top government leaders, directors of major agribusiness enterprises, economists and nutritionists, thus involving both government and business sectors. Since the program will tend to be large in scope and multidimensional in terms of its economic and nutritional impact, costs will be high initially and will continue at a significant level. Although the ultimate effects of a basic shift in agricultural policy are far-reaching, the economic effects of the program, as measured by the availability and cost of given commodities and by annual production statistics for given crops, can be readily compiled.

If carefully planned and not overly ambitious, the program is likely to be implemented in an effective way. The risks in the program are largely of an economic nature; the people can only profit from the greater availability of nutritious, low-cost foods.

b. Micro: Improvement of the diet of preschool children by encouraging the establishment of small family garden plots has a number of advantages:

1. the whole family is instructed in the utility of including specific vegetables and fruits in a wholesome diet;
2. the project is local and requires effort and interest from the family group to be successful;
3. the project is relatively inexpensive and requires few, highly trained personnel; and
4. the effects are long lasting.

Suitable varieties of carotene-rich vegetables and fruits, which are acceptable in foods by the people and may readily be cultivated in a given region, must be chosen. Instruction in the cultivation of such plants including surveillance to reduce losses by pests, incumbent weather or faulty fertilization will be necessary. In addition, an educational campaign must be conducted to insure that a portion of the crop, properly prepared, is ingested by the preschool children in the family.

Some of the problems are: the apathy of families to initiate and perpetuate a project of uncertain economic rewards; the lack of suitable land, as in the urban slums; plant loss by theft or pests; sale or barter of the crop as a commodity rather than its use as a food for young children; and the lack of an immediate effect in groups with high prevalence of vitamin A deficiency.

Agricultural experts and persons knowledgeable in food habits would initially be needed to select proper varieties of fruits and vegetables and to define conditions of cultivation, but thereafter the distribution of seeds and information would be routine. Responsibility for the program in the community must be clearly assigned to prevent a loss of interest. After its establishment, continuation of the program should be relatively inexpensive. One of the major difficulties will be to assess the extent to which locally grown produce is actually consumed by preschool children in the community. Essentially no risks are involved.

Nutrition Education

The health status of the individual in a given population can be improved by introducing nutrition instruction programs into the formal educational system and should reach children of all ages as well as adults. Short-term informal nutrition education efforts should be especially directed toward pregnant and lactating women and infant and child care centers, and toward personnel participating in other strategies devised to improve nutritional and health status. Educational efforts should be part of a continuing long range program utilizing the best expertise available and should be carried on until the literacy level of the population achieves an adequate understanding of the relationship between dietary and health practices and the well-being of the individual. Other than time-tested instructional methods, educational tools and diverse media such as posters, demonstrations, visual aids, radio messages and T.V. programs, should be utilized and integrated toward achieving the common objective.

Socioeconomic Measures

In some cases, vitamin A and carotene-containing natural food sources are readily available or potentially available but their consumption is not equitably distributed among all sectors of the population. This ill-distribution usually has its roots in socioeconomic factors, such as poor purchasing power, low effective demand, inadequate marketing or lack of technology for transportation and preservation of perishable vitamin A containing fresh foods, for example. Correction of these negative factors involves goal-oriented government action, requiring political decision and/or complex input of technical expertise in economic and in the social sciences. The benefits of such actions are expected on a relatively long-term basis. The cost of initiating this type of intervention is variable depending on the sophistication level of the existing sociopolitical intrastructure, but once established the effort can be continued at relatively low cost as part of the national socioeconomic policy. Monitoring techniques are non-specific but can be integrated into the socioeconomic policy of national or regional programs, thereby minimizing their cost.

Factors Influencing Intervention Selection or Characteristics of Interventions: A well-nourished and healthy individual is the ultimate aim of all nutrition programs, including the programs aimed at the reduction of vitamin A deficiency. While the following table (Table I) outlines the characteristics of some possible interventions, the ultimate solution to the vitamin A problem or any other nutritional problem is to insure an adequate intake of proper foods at a cost within the means of the entire population and within an appropriate time interval. This leads to the inevitable conclusion that the food must be available and the economic level of the population must be high enough to purchase the food. Ultimately the solution lies within the economics of a country and its access to an adequate food supply either from domestic or foreign agricultural production. The ease of monitoring the vitamin intake of the population once an intervention program is initiated, should enter into the selection of the adapted program.

Public Health

Public health intervention strategies may include those designed to attack the problem of vitamin A deficiency either indirectly by altering environmental conditions associated with increased need for the vitamin, i.e., acute diarrheal disease and chronic and systemic infections, or directly by utilizing the existing public health systems to deliver the vitamin as part of ongoing programs. Both approaches involve policy decisions by the health sector of the government. These decisions will determine whether the program has an impact upon the general or a targeted population. For example, an immunization program against measles would influence the vulnerable child population while a program to improve distribution of the potable water supply would affect the population in general. Such programs usually require time before a discernable improvement of vitamin A nutriture can be noted. The costs involved in implementing and maintaining these programs will be determined by the nature of the approach chosen. For example, the initial cost of providing a continuous water supply to individual households would be high but the cost of maintenance low, whereas the cost of providing or maintaining nutritional rehabilitation centers would be high initially and continuously. The need for public participation and the personnel required would depend upon the program chosen for implementation. In any case, well-trained public health personnel would be essential to the program. These approaches, although difficult to monitor and less immediate in benefit realization have long range and generally positive effects on health at virtually no risk to the population.

A direct attack on the vitamin A problem is possible through incorporating the vitamin into the existent public health delivery system. This approach would not involve training of additional personnel. For implementation, the approach again would involve policy decisions primarily by the health sector. The financial input required would be minimal since it would essentially involve only the cost of the nutrient. The effective coverage of the population at risk would be limited to those utilizing the available health services and through which there existed contact through community programs. This strategy could be effective and low cost if an extensive health delivery intrastructure exists or the potential for such could be easily tapped, i.e., family planning network into which vitamin A delivery could be inserted; retraining underutilized yaw workers to monitor the nutritional status of preschool children in communities; or rehabilitation centers for

Table I

KEY

H — High; H-a — High (active)
M — Medium; M-a — Medium (active)
L — Low; L-p — Low (passive)
V — Variable; N — None; D — Difficult; S — Simple

Strategy	Population Coverage	Time to Achieve Benefits	Focus	Initial Cost	Continuing Cost	Public Participation	Personnel	Expertise	Initial Effort	Continued Effort	Ease of System Monitoring
Massive dosing	Individually targeted	Very short (days)	Single or multi-nutrient limited	H	H	L-p	H	L	H	H	D
Nutrification	General population or targeted segment	Short (months)	Single (vitamin A) or multi-nutrients	M	L	N	L	H	M	L	S
Macro-horticultural approach	General population or targeted segment	Long (years)	Multi-nutrients	H	M	H-a	H	H	H	M	M
Micro-horticultural approach	General population or targeted segment	Medium (months/years)	Multi-nutrients	M	L	H-a	M	M	H	M	D
Nutrition Education	General population or targeted segment	Long (years)	Multi-nutrients	M	M	M-a	V	H	H	M	D
Public Health	General population or targeted segment	Medium (years)	Program dependent	V	V	V	V	H	V	V	D
Socio-economic Change	General population or targeted segment	Long (years)	Program dependent	V	V	M-a	V	H	V	V	M

malnourished children. If such programs and resources were non-existent, the cost for implementing this strategy would increase very substantially. Monitoring such programs would be difficult. The risks involved would depend largely upon the form, potency and delivery system of the vitamin required for this purpose.

Combined Interventions

From the previous sections, it is clear that each intervention strategy requires a specific set of inputs and has a specific set of advantages and constraints. In the present section, some examples of specific problem situations which might arise and suggested ways of combatting them are defined.

Problem situations are analyzed according to considerations such as: (a) whether or not foods rich in vitamin A activity (carotenoids and vitamin A) are available at reasonable cost in the region where the problem exists; (b) whether or not the prevalence of clinical and biochemical signs of vitamin A deficiency and its sequelae is high enough to warrant immediate action programs; and (c) whether or not the existence of vitamin A deficiency is accompanied by generalized malnutrition and a host of other debilitating factors, such as a high incidence of infections, infestations and other diseases.

Methods of intervention include: the massive dose; nutrification (fortification) of basic food stuffs; horticultural approaches at local and national levels (the establishment of local garden plots for the growing of carotene-rich vegetables and fruits); modification of national or regional agricultural policies, including marketing and food distribution practices; development or strengthening of public health activities. Public health measures include the instructing of public health doctors, nurses, and other health personnel in the signs of vitamin A deficiency, about foods containing vitamin A, about suitable vitamin A nutrition for the pregnant and lactating woman, in the importance of breast feeding for the infant and in the proper selection of post-weaning period foods, as well as insuring the availability of suitable vitamin A preparations in the rural health center. In addition, programs which effect change in the general socio-economic conditions where a problem exists, hence altering the effective demand for vitamin A, offer an indirect method for intervention.

Finally, intervention methods are selected according to their general utility over a short-term, medium-term or long-term period. Certain methods, such as public health measures, nutrition education and some horticultural practices and agricultural orientations should be initiated early in a program and continued until a lasting effect has been achieved, whereas other methods are designed specifically to correct an existing acute problem which, because of its seriousness, requires immediate action.

Vitamin A and carotenoid containing foods may be lacking in a given region because either little or no potential exists for producing such foods, or the potential exists but has not been exploited. Lack of potential might be found in very arid climates, among migratory tribes or where land is not suitable for cultivation. On the other hand, a readily correctable situation may exist where land and water are available but vegetables are not cultivated or used because of tradition. When vitamin A containing foods sources are present and are utilized in a given region, the existence of vitamin A deficiency might be due to improper distribution and utilization of these foods among different sectors of the society, or uneven utilization of these foods within the family. In the latter instance, food practices, taboos and folk concepts of health may play an important role. When the social, economic or ecological reasons underlying a given nutritional problem are well understood, then and only then can suitable measures be defined for resolving the problem in a lasting way. Some possible situations which might arise and strategies for approaching these specific problems are given in Table II.

RECOMMENDATIONS

1. Careful situational analysis is essential before any specific intervention policy is selected. With this analysis on hand, the decision-maker needs clearly to identify his objectives in instituting an intervention and to relate these to associated national policies of the country involved. Then, and only then, is he ready to consider suitable options for problem solving.

2. No intervention can be successful within a given country unless from its inception it fits

TABLE II
Situations and Indicated Potential Interventions*

Situation Components of Problem						Interventions Range**		
(1)	(2)	(3)	(4)	(5)	(6)	Short	Intermediate or Long	
Yes	Yes	No	No	Yes	Yes	I, II	IIIb	IIIa, IV, VI
Yes	Yes	No	No	Yes	No	I, II	IIIb	IIIa, IV
Yes	Yes	No	No	No	Yes	IIIb, II	IV	IIIa, VI
Yes	Yes	No	No	No	No	IIIb, II	IV	IIIa
Yes	No	No	No	Yes	Yes	I, II	IV	VI
Yes	No	No	No	Yes	No	I, II	IV	IV
Yes	No	No	No	No	Yes	II	II	VI
Yes	No	No	No	No	No	II	IV	
No	Yes	Yes	No	Yes	Yes	I	IIIb, VI	IIIa, VI, V
No	Yes	Yes	No	Yes	No	I	IIIb, V	IIIa, IV
No	Yes	No	Yes	Yes	Yes	I	IV, IIIb	IIIa, VI
No	Yes	No	Yes	Yes	No	I	IV, IIIb	IIIa, IV
No	Yes	Yes	No	No	Yes	II	VI, V	IV, IIIa
No	Yes	Yes	No	No	No	IV	IV	V, IIIa
No	Yes	No	Yes	No	Yes	IV	IIIb	VI, IIIa
No	Yes	No	Yes	No	No	IV	IIIb	IIIa

**Explanation to codes for components of problem (Arabic numbers) and interventions (Roman numbers) appear below.*

***Time also has a connotation of priority.*

Situation Components of Problem. Code to Table II

1. Lack of natural food vitamin A sources.
2. Potential for increasing natural food vitamin A sources.
3. Improperly distributed and consumed by different sectors of population.
4. Improper intrafamilial distribution and consumption (especially affecting the small child).
5. Important incidence of severe clinical and biochemical signs.
6. Important secondary contributing factors (diarrhea, infections, poor overall diet).

Intervention Code for Interpretation of Table II

I. Massive dosing
II. Nutrification
III. a. Macro-horticulture
b. Micro-horticulture
IV. Nutrition Education
V. Socio-economic Approaches
VI. Public Health Approaches

within government policy and the means exist for its implementation and monitoring to a successful conclusion.

3. Although some interventions afford immediate benefits and are important to implement when a serious clinical problem exists, they may be a temporary and partial solution. It is recommended, therefore, that such action be combined with a second strategy which offers a more permanent solution to the basic underlying problem. The Task Force believes that combined approaches are most likely to succeed.

4. Evaluation must be made both during and at the conclusion of the program to judge what measure of success is achieved.

5. The Task Force realizes that strategies other than those listed in this document may now exist, be in the developmental stage, or emerge in the future. Support should be given to these efforts both while in the early stages of development and when ready for wide scale field-based testing.

6. Food imported into a developing country for consumption by a population with a known nutrient deficiency in their diet, should contain the missing nutrient when economically feasible.

III.
EVALUATION OF SELECTED VITAMIN A INTERVENTION STRATEGIES
IVACG Task Force on Evaluation

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INTRODUCTION

The ultimate solution to vitamin A deficiency and its associated clinical syndromes, including xerophthalmia and resulting blindness, is for all populations to enjoy daily a diet containing fully adequate levels of vitamin A, as well as other essential nutrients which interrelate for normal utilization. The need for and the existence of a variety of programs or actions, all related to correcting the problem of vitamin A deficiency in population groups in many countries, is recognized. One of the problems often connected with these programs, that limits the potential for general application and maximum beneift, however, is the lack of appropriate schemes for evaluation of success and cost-effectiveness. We consider that a main cause of this problem is the lack of an appreciation of the need for evaluation and of a well-defined methodology by which it can be implemented. It is the purpose of this paper, therefore, to address this issue.

To assist the reader, some clarification of evaluation terminology as applied in this paper is in order.

Evaluation is the process of determining the value or amount of success in achieving a predetermined objective using clearly defined criteria.

The *purpose of the evaluation* of any intervention program is to provide a factual basis for decision making in establishing priorities for use of resources within a political context. The distinction between *evaluation* and other kinds of *research* is that evaluation does not seek new knowledge but attempts to assess progress towards prestated objectives, usually achieved via organized "programs."

A program is a set of activities which have specific inputs of resources and conditions, organized and processed to accomplish an end and which can be evaluated against certain standards. Evaluation of the *success of any program* must be based on evidence of change from a baseline condition considered undesirable toward a preset goal and at what cost, both socially and economically.

The Task Force in preparing this paper has made two general assumptions.

1. that the problem has already been defined according to the assessment criteria for a public health problem previously outlined in this document and that this definition will serve as a baseline. If all of the essential parameters for evaluation of a *specific* intervention program have not been included as a part of the definition-assessment phase, it may be necessary to obtain additional quantitative baseline information;

2. it is further assumed that an appropriate intervention strategy has been selected and designed to address the problem, according to methodology described elsewhere (Task Force II).

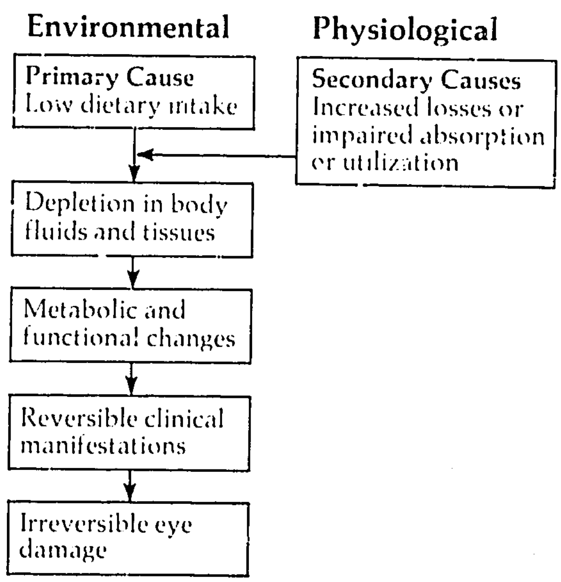
PROCESS OF EVALUATION OF INTERVENTION STRATEGIES

Program Goal Definitions

The Task Force considers that hypovitaminosis A is a problem with undesirable consequences to health, such as inadequate growth and development and decreased resistance to infection, as well as ocular lesions (xerophthalmia) and blindness.

The simplified diagram that follows is presented to illustrate this point through a conceptual review of the natural history of vitamin A deficiency. It is suggested as a framework from which to identify at what points specific program strategies might be intervened.

We recognize that a comprehensive attack on



the problem ideally should include measures to eliminate or reduce both the primary and the secondary causes of vitamin A deficiency. However, a basic working tenet is that marked improvement in dietary intakes of biologically utilizable vitamin A will by itself contribute significantly to the solution of the problem. Interventions to reduce or eliminate the effects of the secondary causes are most important but are considered beyond the specific charge to this Task Force.

Most vitamin A intervention programs currently under consideration are directed towards the two following goals:

Goal 1: Programs to increase the intake of vitamin A and pro-vitamin A and consequently to improve the vitamin A nutritional status of a population.

Goal 2: Programs to prevent irreversible eye damage.

Programs to increase vitamin A intake and improve vitamin A status: A certain intake of vitamin A (retinol equivalents) by humans is essential in order to insure an adequate supply to the tissues, thus permitting normal metabolism and function. Several international and national expert groups, after reviewing the evidence available, have proposed recommended intakes of vitamin A which to the best of their knowledge are compatible with good health.

Many populations who are under ecological and socioeconomic constraints and who are characterized by an unsatisfactory status of health do not consume these recommended intakes. This fact has been accepted as the rationale for a variety of programs intended to raise the vitamin A intake of populations to at least the recommended levels. The purpose of these programs should be to insure that no member of the population consume less than an adequate intake of vitamin A. Since low intakes of vitamin A result in decreased concentrations in body fluids and tissues, the long range goal of these interventions is to increase the vitamin A status of these individuals to the level that characterizes adequately nourished groups. The evaluation of such a program scheme should therefore include determination of the extent to which the recommended levels of vitamin A *intake* is reached, and the extent to which the program impacts on achieving adequate vitamin A status as measured by biochemical, clinical and dietary intake parameters.

Programs to prevent irreversible eye damage: The social cost to individuals and society, because of loss of sight due to severe lesions of the eye caused by vitamin A deficiency, has been the stimulus in many countries for undertaking preventive intervention measures. These programs are directed especially toward the goal of total elimination of such preventable blindness in the population. The Task Force recognizes that this objective is directed towards one late stage within the broader problem of low levels of vitamin A in a total population as described above.

The design of intervention programs to achieve the reduction of xerophthalmia and the often resulting blindness, therefore, will have different characteristics to be taken into account. For instance, these characteristics will include a target age group in the population (generally accepted to be 6 months to 6 years), association of the specific nutrient deficiency with other manifestations of an overall malnutrition problem and the correlation with low socioeconomic conditions. In general, however, the same methods of evaluation and standard biochemical and clinical criteria of effectiveness are suitable to measure success.

Criteria for Measuring Program Effectiveness

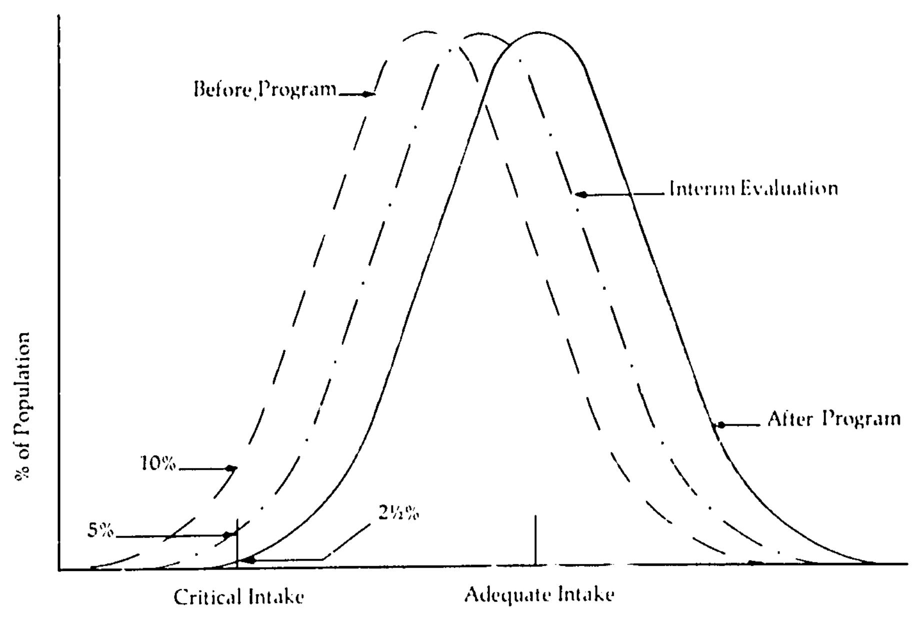
Evaluation of the success of any program must be based on evidence of change from the baseline undesirable condition and the cost socially, politically and economically. Recognition must be given to the fact that change is a dynamic process and that progress toward program objectives needs to be evaluated against predetermined intermediate targets within a defined time frame. Premature judgements about program success should not be based on intermediate target evaluations.

As stated earlier, one goal of intervention strategies (Goal 1) is to raise the level of vitamin A intake to that recommended as adequate for health. The intake recommended as adequate will vary somewhat according to the reference standard used, i.e., FAO/WHO, UK, or PAHO, for example. For the purpose of this paper we have adapted the figures of the FAO/WHO expert group to various age groups as shown in Table I.[1] In many populations a certain number will not consume an adequate intake. Systematic observations on deprived adult humans indicate that the critical intake to prevent metabolic and clinical evidence of deficiency is about 50 percent of the intake recommended for adults, as shown in Table I.[2,3] This estimate is based on limited experimental data[1] and this minimal intake value is a fair but rough estimate, "about 50%" or "about half," is a more judicious statement. It should not be interpreted as an absolute one below which clinical disease will occur. Nonetheless we have chosen to apply this percentage to the recommended adequate intake level for all the specified age groups in order to arrive at a critical minimal intake level for purposes of program evaluation. It is suggested that programs with Goal 1 should aim at reducing the proportion of a population, with intakes which fall below the minimal critical level, to less than 10 percent.*

**This criterion is believed to be reasonable since dietary intakes are generally difficult to quantitate, particularly when dealing with a large sample. The value is adopted from the FAO/WHO Report, Expert Group, Table I.*

TABLE I
Criteria for Evaluation of Program Success
Vitamin A Intake

Age Group	Adequate Intake (retinol equivalents in μg/person/day)	Critical Intake[1] (retinol equivalents in μg/person/day)
0-6 mo.	420	210
7 mo.-6 yr.	300	150
7-9 yr.	400	200
10-12 yr.	580	290
13 yr. +	750	380



1. Specifically established for targets to be determined by program designers for the acceptable magnitude of change from critical condition expected within a predetermined time period.

An adequate dietary intake of retinol equivalents generally is associated with an adequate level in physiological fluids and tissues, assuming the intake is biologically available. The feasibly available body fluid for assessing bioavailability of dietary vitamin A and of tissue stores is blood. We recognize the limitation of this fluid in measuring *relative* vitamin A nutriture, except in cases of severe depletion, and when assessing the distribution of blood values among large population groups. For the purpose of *program evaluation* it is important to look at *population distribution curves* for serum vitamin A values.

Blood studies on different age groups have suggested an age relationship, at least, for the first few years of life. Distribution curves for children under about six, therefore, should be considered separately from those of adults. Consequently, mean serum levels considered adequate and compatible with health will be somewhat lower for young children than for older age groups.

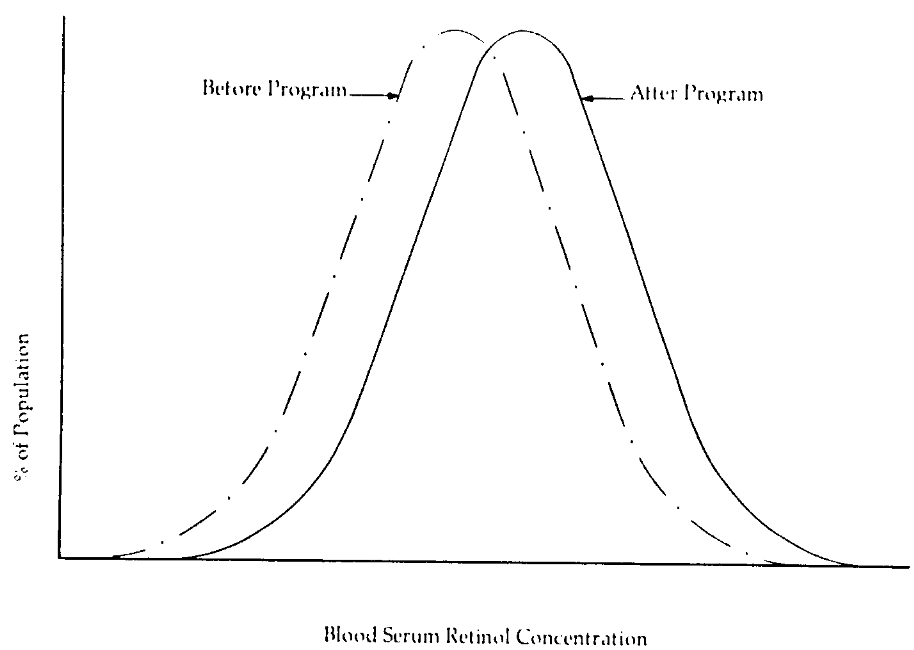
Evaluation of published data on *population*

TABLE II A
Blood Serum Retinol as Indicator
Criteria for Evaluating Program Success

Adequate
20 μg/100ml

Critical Limit
10 μg/100ml

Indication of program success[1]



1. Percentage reduction of prevalence of critical level to be specifically established by program designers within a predetermined time period.

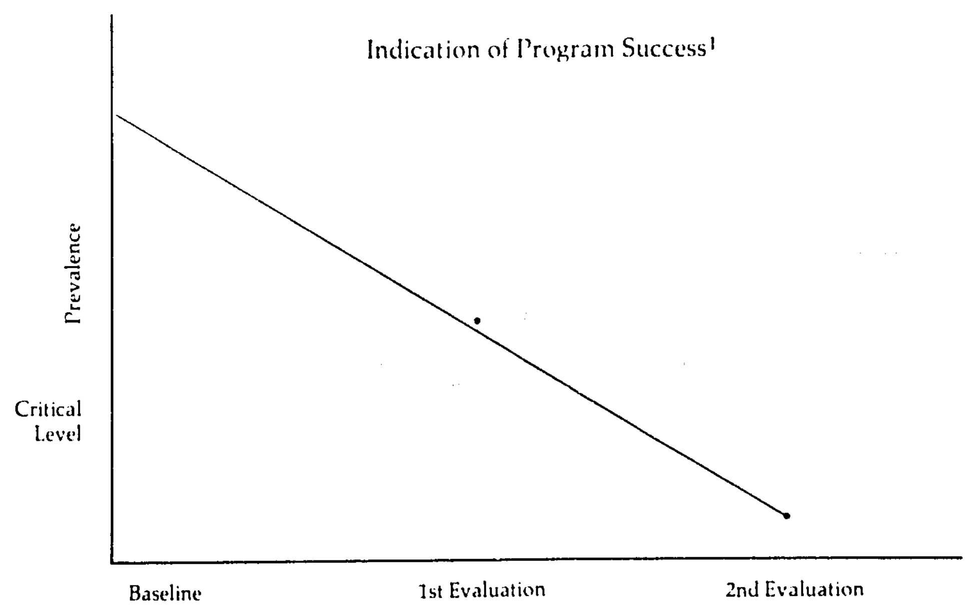
known to be free of significant vitamin A problems and consuming adequate intakes (at least at the level listed in Table I) indicate that less than 15 percent have serum levels below 20μg/100 ml of which less than 5 percent are below 10 μg/100 ml. Critical levels indicative of risk of clinical deficiency are 10 μg/100 ml. However, it is suggested that an undesirable condition exists if values less than 20μg/100 ml are found in 15 percent or more of the population. A reduction in the prevalence of values in this range of the distribution curve should be an intervention program goal.

Recently it has been proposed to determine vitamin A in breast milk as an indicator of the vitamin A status of the mother and as an index of the dietary intake. Its potential as one tool to assess program success in raising the intake of bioavailable vitamin A sources should be considered.

Levels of vitamin A in the liver of accidental death victims collected before and sometime after introducing a program have also been suggested as a means of evaluating change in vitamin A status of populations. Again, al-

TABLE II B
Clinical Eye Damage

Clinical Lesion	Adequate (percent prevalence)	Critical Level (percent prevalence)
X1B	0	2
X2 + 3A + X3B	0	0.01
XS	0	0.1



1. Percentage reduction of prevalence of critical level to be specifically established by program designers within a predetermined time period.

though this tissue is the best reflection of true relative status, this is not always a practical method, since most developing countries would not have the resources to perform determinations under well standardized conditions.

For the second goal (Goal 2) of intervention strategies (to eliminate all blindness associated with vitamin A deficiency), we agree with the criteria as set forth in the report of the Assessment Task Force and recommended by the AID/WHO sponsored Jakarta meeting which defined the level of prevalence of clinical and biochemical parameters indicative of a public health problem. These criteria are given in Table II. The selection of these ocular signs was based on the fact that they are easily recognized, can be objectively quantified and are highly specific. To determine more precisely the etiology of cases of corneal destruction presumed to be related to vitamin A deficiency, the criteria suggested by the Assessment Task Force should be followed.

For the purpose of program evaluation, and having established the criteria for determining the baseline conditions in a population that are considered undesirable, each intervention strategy should include episodic evaluation against predetermined, specific intermediate targets. The evaluation should also include the components of the specific intervention strategy and how these might be expected to interrelate to produce measurable benefits.

Reasonable intermediate targets might be set at a reduction by some 50 percent of the number falling in the critical category for one or more of the parameters in Tables I and II. In practice, this approach recognizes progressive change following program implementation and between intermediate evaluations targets. The hope would be for at least a logarithmic reduction in the number falling in the critical level categories. Since some few values always can be expected to be there, programs should not be considered *failures* if some remain in these categories.

One way of expressing intermediate progress in achieving program goals is to express the data in a series of distribution curves resulting from each successive evaluation as illustrated in Tables I and II.

Program Component Analysis

The Task Force believes that after the establishment of the program objective within the framework of the long-range goal, a necessary next step in the evaluation process is to delineate the essential components of the intervention selected to achieve the objective, then to determine questions to be answered about each component in the evaluation. This will permit the evaluation sharply to pinpoint, at the operational level, factors affecting the success or lack of it in the program. In order to illustrate this step, alternative appropriate interventions to accomplish Goals 1 and 2 might be analyzed as follows:

GOAL 1

Raise vitamin A nutritional status

- Fortification
- Public Health Measures
- Horticulture
- Nutrition Education

GOAL 2

Prevent irreversible eye damage

- Massive Dosing
- Fortification
- Public Health Measures
- Supplemental Feeding
- Nutrition Education

Suppose, for instance, *fortification* is selected as the intervention for Goal 1. The major components of this system of increasing the intake of vitamin A as laid out in the program design are identified: (a) the vehicle; (b) the fortifying agent (vitamin A); (c) processing; (d) the delivery system (marketing and distribution); (e) consumption pattern.

Questions to be answered by an evaluation might be:

(a) Is the amount of vitamin A in the vehicle adequate to raise the level of intake sufficiently to improve the biological status?

(b) Does the established processing method for fortification result in an effective product?

(c) What degree of the population is reached by distribution through the existing marketing system?

(d) Do various groups in the population consume sufficient of the fortified vehicle to obtain desired effects?

Or, suppose massive dose vitamin A distribution is selected as a means of eliminating blindness in a preschool child population. The major components are: (a) the vitamin A oral dosing vehicle (capsule or liquid form); (b) the organizational network through which the dosage flows from source to consumer; (c) the intrastructure of operational personnel—its training and functioning; (d) facilities required—including transport, storage, registration forms; (e) populations receiving the vitamin A supplement.

Questions might fall into two large areas: (a) How well do the organizational arrangement, personnel and facilities operate to reach the maximum number of recipients? (b) Does the dosage of the amount of vitamin A distributed to the target population significantly reduce the incidence of xerophthalmia and of blindness? In other words, the desired result of a program as measured against certain criteria may be effected by one or more of the components so that the judgment of the effectiveness of the total program must be qualified.

Once having delineated the components and drawn up the questions relating to each, it is essential to establish the steps in the total process (and in each of its components) in order to identify at which point the process or component is ineffectual or malfunctioning. The proper sequencing of the evaluation activities is important for valid measurement, keeping costs in mind. Clearly, the scheduling of the assessment of different components of the interventions will vary. For instance, if evidence exists of a breakdown in the marketing and distribution system of a fortification program, there is little point in concurrently sampling the population in order to determine vitamin A status of dietary intake.

Data Collection and Program Adjustment

The data collection stage should only proceed after the program objectives, components and criteria for measuring success have been identified. In the past, intervention programs have sometimes been initiated without adequate baseline studies upon which to gauge progress. In such instances, control studies in a population from a similar geographic area with similar ecological and socioeconomic characteristics have been used for comparison with the intervened population. The sensitivity of such cross-sectional comparison is considered to be less than a *before and after* comparison in the same population.

Having identified the components of the program and formulated the question to be answered on each, instruments must be developed to obtain data to be analyzed as a basis for measuring progress or lack of it. A systematic process of obtaining essential information should be put into a form to fit eventual needs. It can then be presented in a format which permits evaluation of progress towards the stated goals at set intervals. This process should permit intermediate adjustment of programs when obstacles and constraints are pointed up and are amenable to change to produce more effective program functioning. This, therefore, is seen as a dynamic process which feeds back information allowing adjustments in program activities as indicated

Data Analysis and Determination of Degrees of Effectiveness

The analysis of the data collected for evaluation of the components will depend upon the specific component under consideration. For example, the analysis of data on the effectiveness of four of the five components of fortification as outlined under program component analysis is straight forward (a, b, c and e). On the other hand, market and distribution analysis (d) will require a combination of descriptive and statistical techniques which are somewhat a function of the structure of the market under consideration. Clearly a statistician should be consulted to assist in designing the most effective evaluation scheme. The evaluator has to be well aware of the possibility that the effect of variables independent of the intervention per se may be confounding the interpretation of the cause-effect relationship of the program. For example, as social and economic conditions in general improve, decreased prevalence of A deficiency may occur independent of a specific intervention strategy. This is an especially important consideration in the course of programs of long term duration.

Economic Analysis of the Project

The estimation of costs and benefits of any intervention program requires the assistance of an economist familiar with the application of cost-benefit techniques. The discussion in this paper outlines the general circumstances surrounding such an evaluation. It must be emphasized that the problem of not being able to place monetary values on all of the benefits of intervention will challenge the ingenuity of the evaluators.

The calculations of the costs and any comparison with benefits is done most usefully by recognizing that the value of money changes with the way it is invested or used over time. Simplistic formulations such as total annual costs divided by population protected in a given year, or on the average since the inception of the program, do not capture this notion. They may show a program whose costs are high in the initial years as very ineffective when in fact the benefits can only be measured after a lapse of time. Alternatively a program with low initial costs but few *down-the-road* benefits may appear in a more favorable light. The notion of "discounted value" may be used to avoid these difficulties. Typically, cost-benefit or internal rate of return are the techniques to be used. The cost per person protected, to the extent that it can serve as a useful indicator for policy makers, could also be calculated on a discounted cost basis.

The obvious source of benefits from vitamin A intervention programs are both from cost savings and from increased productivity resulting from improved health status. Costs are saved in health care particularly for treatment in service of the blind. Increased productivity of the work force, although difficult to quantify, will contribute directly to the national input. Less obvious, and even more difficult to quantify, is the greater enjoyment of life and fulfillment from life which accompanies good health. The difficulty in placing monetary values on improved general health status and particularly on human sight, does not negate the value of economic analysis of the project.

Given the difficulties in quantifying benefits, cost-benefit techniques may be most useful in:

1. Choosing those programs which provide equal or similar benefits at lowest costs;
2. Identifying all cost components of the program; and
3. Providing information for financial management by identifying cost streams through time.

The emphasis in analysis is not to generate cost-benefit ratios to justify a program, but rather to select that program or programs which will provide a desired level of vitamin A intake at the lowest cost to society.

In order to estimate the cost of an intervention strategy the following path may be followed:

1. Specify the program duration (time-frame);
2. Determine the *cost* of program inputs on an annual basis and calculate the cost streams, including: (a) training costs, (b) personnel, (c) facilities and equipment, (d) materials, (e) monitoring costs, (f) other;
3. Determine the *number of persons "protected"* by a comparison between the number of persons in the critical level category (defined in the *criteria for measuring effectiveness*) before and after the intervention. (This can be the basis for evaluating the benefit stream.)

Identification of the cost streams associated with any program, although not simple, is relatively straight forward. This alone could provide the basis for choice between alternative intervention strategies with similar goals, as well as for individual program assessment.

The benefits are, as already noticed, more difficult to quantify, given the problems associated with evaluating the economic value of improved health status. Nevertheless, careful identification of sources of benefits would assist policy makers in program evaluation and selection.

The methodology outlined here requires a careful identification of annual resource requirements. This is necessary for budgetary analysis and planning. The use of the cost-benefit technique would also require careful specification of intermediate program outputs and thus serve as a basis for periodic program evaluation. Periodic evaluations will provide policy makers with the opportunity to adjust program techniques and management to changing country circumstances.

The cost of the evaluation procedures should rightly be included as program costs in some instances. The judgement of the program designers will be required here.

Selection of the time period for evaluation requires precise consideration. The initial time phase is the period to develop and mount the operation of obtaining the baseline and monitoring system. The time phase of the flow of feedback, which forms the basis of analysis, will be dependent on the elements of the delivery system and its estimated critical period for detectable change. An economist should be assigned to work closely with both program planners and evaluators.

RECOMMENDATIONS

1. It is recommended that an evaluation scheme be built in at the outset of program planning, drawing on appropriate multi-disciplinary expertise.

2. It is further recommended that, insofar as possible, this evaluation expertise be drawn from national resources in order to strengthen in-country capabilities and insure the continued interest in monitoring of and general surveillance of program activities. National experts are generally better equipped to interpret and make adjustments in light of local conditions.

3. It is recommended that two distinct phases of the evaluation process be identified: *an intensive initial evaluation phase* and an ongoing *monitoring process*. The time of the initial phase is determined *a priori* in accord with the characteristics of the program on the basis of the predicted time which will be required to produce the expected change. Once the initial phase is finished, and if the program is to be continued, a careful analysis must be made in order to select from the complete battery of measurements of the initial phase, those which are contributing the most critical information at the lowest cost and effort. With this reduced battery of practical indicators, the surveillance or monitoring scheme should be designed for continuous application throughout the duration of the program. The information obtained through this surveillance scheme should be fed back to the program managers for use in supporting the continuation of the program, its modification or its termination, depending on the results.

4. Some programs may have been undertaken or have emerged as a result of informal activities which became organized, without an earlier evaluation as a baseline. Desirable as the retrospective evaluation of effectiveness of such programs is, the retrospective evaluation is difficult. Estimates of the degree of effectiveness of these programs as a basis for decision on continuation, adjustment and/or replication in other areas can only be tentative. This must be recognized in view of the possibility that the results of such as assessment might be negative and unpopular.

5. It is recommended that the results of program evaluation be disseminated as widely as possible, in order to reduce duplicating efforts and costs, and to stimulate new programs where needed. Dissemination of results is generally of much practical interest. The information and experiences obtained should be presented as reports with full details on the findings, interpretations, conclusions and recommendations. Because of the interest of other countries or regions where vitamin A deficiency is still a public health problem, regular publication and communication channels, such as scientific congresses, should be used.

6. It is recognized that a comprehensive *evaluation* of an innovative program to reduce or control vitamin A deficiency, as an essential component in a program, requires a considerable outlay of funds. Such a prospect might prove a deterrent for deciding to introduce an intervention. This Task Force, which endorses in principle a built-in evaluation component in any new program, nonetheless, would not want to inhibit remedial efforts to attack the problem where it is known to exist. Under these circumstances, it is recommended that efforts be made to select some critical indicators that could evaluate the effectiveness of the program at minimum cost.

7. Whereas the three task forces have made a considerable contribution by producing guidelines for the determination of the extent of the problem of vitamin A deficiency in a population, the evaluation of intervention strategies for remedial action, and the areas to be researched for additional knowledge, there is an obvious

gap which needs to be bridged between the identification of the problem and assessing the means of problem solution. It is, therefore, recommended that guidelines be developed in the near future for the *methodology* and *process of selection* of appropriate interventions for analyzing alternative options and patterns of operation for program selection, and for designing a program to correct the specific problem. This process should consider the nature, magnitude and distribution of the problem, including existing social, economic and political realities, as well as the availability of resources—financial, material and human.

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IV.
RESEARCH NEEDS IN PRESENT AND FUTURE VITAMIN A PROGRAMS
IVACG Task Force on Research

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GUIDING PRINCIPLES

The objective of the Research Task Force of IVACG is to designate areas of research and its application within developing countries in order to advance the overall goal of eliminating vitamin A deficiency in populations around the world by preventive and therapeutic practices. Vitamin A is an essential nutrient for mammalian life. It is not synthesized within the body and hence, since the beginning of man, has been provided in variable amounts as a component of his diet, either in the form of true vitamin A or as carotenoid vitamin A precursors. The Research Task Force believes that the ultimate solution to vitamin A deficiency and its associated deficiency syndrome, xerophthalmia and resulting blindness, is for all populations to enjoy a daily diet containing a fully adequate level of vitamin A as well as its interrelated nutrients such as protein, zinc and iron. High priority should be given to intervention practices or nutrient delivery systems aimed at immediately or eventually providing an adequate intake of these nutrients. As an interim prophylactic measure the Research Task Force recognizes the immediate advantages of intermittent high-level vitamin A dosing, even with its limitations. These include: not covering 100 percent of vulnerable members of a given population due to the need for individual administration of the dose at critical time periods, and the idiosyncracies of efficacy as influenced by malnutrition, emesis and diseases of respiratory and gastrointestinal tracts and intestinal parasites. It is a worthy practice even with these limitations. Critical in the objective of the Research Task Force is the treatment of vitamin A deficiency when the symptomatology is so advanced that the saving of sight and the cure of xerophthalmia can best be approached by the combined use of water-dispersible vitamin A parenterally administered by intramuscular injection followed by a program of oral dosing of vitamin A. This should be in combination with a diet containing an adequate level of high quality protein and also rich in carotene and/or vitamin A. In order to avoid a recurrence, this type of diet should continue beyond the period of treatment.

RESEARCH ON INDICATORS OF NUTRITIONAL STATUS

In investigating a given population, biochemical, clinical and dietary indicators of significance are the keys to laying the ground work for subsequent decisions. At present, several biochemical methods are variously employed for the assessment of vitamin A nutriture, but there is not general accord as to the optimal procedures. Further research is warranted here.

Biochemical

Recommendations:

1. Standardized methodology should be established for the collection of tissues, their storage and particularly the assay of these tissues (blood and liver) for vitamin A.

2. Retinol-binding protein (RBP) is an influencing factor in the transport of vitamin A in the blood. Investigations should be undertaken to determine whether the measurement of retinol and RBP and/or vitamin A/RBP ratios might be a helpful tool in assessing populations for vitamin A nutriture.

3. Based on the work of several investigators, it appears that vitamin A metabolites are excreted in urine and that these may prove useful in assessment of vitamin A nutritional status. Support for further studies is justified, better to define and to quantity these excreted metabolites and to ascertain whether they may serve as the basis of a useful measurement of vitamin A nutriture in man.

Clinical

The clinical criteria used for xerophthalmia classification have been agreed upon and are contained in the Report of a joint WHO/U.S. AID meeting on "Vitamin A Deficiency and Xerophthalmia." There are five clinical areas in which research needs to be undertaken.

Recommendations:

1. Night blindness. It is known that a diminution in the supply of vitamin A to the rod cells of the retina leads to an impairment of the function of dark adaptation. This results in night blindness which may be noticed by older children or adults themselves, or may be reported to the investigator by the mother or

guardian of a young child. At the present time no simple field test exists which can objectively measure night blindness. If such a test existed, this would be an enormous step forward in the surveys designed to assess vitamin A nutriture.

Methods currently in use are rod scotometry, dark adaptation tests and electroretinography, all of which may be used to detect reduction in dark adaptation in the early stages of night blindness. However, none of these methods are applicable in the preschool age child and under field conditions.

The development and testing of a relatively simple, yet sensitive, test of rod function, a method of demonstrating night blindness applicable to young children at risk of xerophthalmia, would provide an importnat advance in measuring the extent of night blindness and hence the subclinical vitamin A deficiency in a population.

It should not be beyond the ingenuity of persons knowledgeable in the physiology of vision to devise such a test in collaboration with ophthalmologists and nutritionists working on the problem of vitamin A deficiency. Such efforts should be encouraged.

2. Objective assessment of xerosis conjunctivae. It is agreed that conjunctival xerosis is an important sign of xerophthalmia, and its presence in a child receiving a diet deficient in vitamin A indicates that destructive eye lesions may soon result. Conjunctival xerosis, although frequently reported, is notoriously difficult to judge objectively, and even trained observers frequently experience differences of opinion relative to its diagnosis. It has recently been suggested that a staining technique (using Rose Bengal or other stains) may help in objectively measuring conjunctival xerosis. This method needs controlled testing by different trained workers under several and varying conditions.

3. Bitot's Spots. These signs usually consist of a small plaque of foamy or cheese-like material, grey or silver in color, on the bulbar conjunctiva. They are generally quite easy to recognize. Bitot's spots are known to be associated with vitamin A deficiency especially in the young child, but are not a necessary stage in the progression of the disease. Because the lesions are easy to detect it would be useful if their significance could be better defined. Since such study is not given a high priority, it is recommended that it be undertaken in conjunction with some larger investigation of the vitamin A problem.

4. Taste impairment and color discrimination. There have been reports that there is a loss in the ability to perceive certain tastes among experimental rats suffering from vitamin A deficiency. It has been hypothesized that this may also be true in humans. It is suggested that a small study be conducted to determine whether this finding is relevant in detecting human vitamin A deficiency. A possible limitation is that taste acuity is most difficult to measure in the very young children who are at greater risk for vitamin A deficiency. Similarly, it has been suggested that visual color discrimination may also be reduced in vitamin A deficiency. This too may warrant investigation, but again may suffer some of the same difficulties as does work on taste discrimination. Techniques and methodology for these procedures are not simple to devise, and it is imperative that any research work undertaken be very discriminating in the choice and use of methods, and should draw upon experts with specialized knowledge in these areas.

Dietary

The investigation of dietary regimes of populations or groups contributes to the establishment of the usual intake of vitamin and pro-vitamin A. There has been a tendency in the past to utilize detailed dietary family studies in investigations of vitamin A deficiency. There is need for an innovative method of obtaining the most pertinent information relative to the inclusion or omission of vitamin A rich or carotene-containing foods in the diet of the child. Similarly, in the evaluation of an institutional diet, such as one in an orphanage, examination of purchase records plus observations of food preparation and serving, by an experienced, alert observer, may provide a useful index of the dietary supply of the vitamin. Development of techniques for useful, simplified dietary appraisals of these types should be encouraged. Food composition tables for regions in countries do not necessarily represent the correct pro-vitamin A level of local foods, particularly as the foods are consumed. The data presented by composition tables were in a large measure developed when techniques for the analysis of beta carotene and its isomers were not as exact as they are today, and in many cases, composition tables represent carotenoid contents of raw (not ready-to-serve) foods. Thus, such tables do not reflect the actual content in the food of pro-vitamin A. In other cases, the data are often developed for varieties of fruits and vegetables as a general class and may not represent what is consumed in a particular region.

Recommendation: In order to make dietary surveys maximally useful, research is required to establish the actual consumption levels of vitamin A and beta carotene and the biological availability of pro-vitamin A of the food "as consumed." This requires the development of improved, simpler methodology adaptable to field surveys, of better methods of preserving samples of food collected for analysis "as eaten," and the measurement of the bioavailability of pro-vitamin A of locally consumed fruits and vegetables. It is imperative that the methodology developed be able to distinguish and estimate the concentration of the neo-carotenoids (cis-carotenoids) and other compounds closely related to beta carotene, including bioavailability studies.

It is important to establish a reference laboratory for developing and standardizing such procedures, and for the collection of data on varieties of foods indigenous to regions of the world experiencing vitamin A insufficiencies.

RESEARCH ON INTERVENTIONS

Nutrification (fortification)

The prophylactic approach to eliminating vitamin A deficiency is favored over therapy. Prophylaxis is best accomplished by providing an adequate supply of vitamin A in the diet. Nutrification of one or more commonly consumed foods with an appropriate level of a stabilized form of vitamin A has the advantage that it reaches all age groups who consume the food items and does not necessitate the long delays required to change the dietary pattern among the population. The principal problem is to find foods which are widely consumed by children in the susceptible age group, which vary slightly in the amounts consumed per capita, and are processed in a plant where quality controlled nutrification is feasible. At the present time, the nutrification of cereal grain products, sugar and tea is taking place in different parts of the world. In one country the incorporation of dry form of vitamin A with monosodium glutamate is under trial. A well-developed technology exists on the addition of vitamin A to many types of foods. Studies of the dietary prophylactic approach should have high priority.

Recommendations:

1. In countries where vitamin A deficiency is a problem, proper surveys should be undertaken to determine which foods may be potential candidates for nutrifying with added vitamin A, even if intermittent high-level dosing is already practiced. A food of high protein content would be preferred. These foods may be consumed in the home or at child feeding centers. Where existing technology does not provide for the incorporation of added vitamin A to the more commonly consumed foods, studies should be undertaken to determine the most feasible method of fortifying the diet.
2. Under certain conditions where nutrified foods are not available, it is possible to prepare a wafer, cube or tablet providing enough vitamin A for an average family. This method has an advantage in that other nutrients absent from the local diet may also be incorporated. When added by the mother of the family to the daily stew, beverage or other food the nutritive value of the diet will be appropriately augmented. This latter approach requires a special nutritional education program and periodic monitoring. The technique deserves rigorous field testing (research) in appropriate locations.

Intermittent High-Level Dosing

Intermittent high-level vitamin A dosing of population segments is not a new concept. It has been in limited use for over ten years. Basically the concept rests upon the physiological principle that a high percentage of a given large oral dose of vitamin A will be stored in the liver and released into the blood, combined with retinol-binding protein as required by the tissue sites. It is an interim measure, and where diligently administered to individual children over a scheduled time period, has been a successful means of prophylaxis. This development was considered *in extenso* in the report "Vitamin A Deficiency and Xerophthalmia" of the joint

WHO/U.S. AID meeting in Jakarta.

There is continuing need for operational research to improve the effectiveness of high level dosing programs as these are extended into large scale field operations. Improved efficacy of this measure may also be achieved by research on matters that pertain to enhancing the absorption, utilization or storage of the administered dose. In some instances it may be hypothesized that absorption of various vitamin A preparations could be limited by gastrointestinal function. In this regard studies would be useful to determine whether growing children, ages 1 to 6 years, easily hydolyze the large dose of vitamin A esters for ready absorption and how this may vary in malnutrition and other disease states. If absorption proved to be limited in some situations, the formulation of the prophylactic capsules could be altered with respect to the proportion of retinol and its esters contained therein, or by the incorporation of an emulsifier to compensate for biliary insufficiency or malfunction.

The merits of single dosing versus divided dosing and the optimal dosing interval need to be further investigated in young children. Also, additional study of optimal field delivery systems that will reach as near to 100 percent of the children at risk and at the lowest unit cost is required.

The degree of liver storage of vitamin A, whatever manner of high-level dose is given, is of course highly important, and hence better understanding of factors influencing storage is of vital concern. Factors requiring greater classification include the age of the child, his disease state, state of vitamin A deficiency, protein malnutrition and the influence of interrelated nutrients.

Having attained maximal vitamin A storage, we still need to gain an understanding of how best to prolong this storage over a period of time in order to protect the subject from vitamin A deficiency. Hence a study of determinants of the rate of release of stored vitamin A from the liver and the factors influencing the turnover rate within the body is needed. The role of the kidney and determinants involved in excretion in the urine are also relevant.

Recommendation: Because there is growing concern over the efficacy of intermittent high-level dosing of vitamin A to children in large scale field trials, further research is needed to understand better the mechanics of absorption, storage, transport and excretion of vitamin A supplied in this manner. There must be efficient means of identifying the child in the field receiving massive vitamin A dosing and the number of doses received per year in order to judge the value of this regime at subsequent periods of assessment.

Treatment

Adequate studies of the optimal dose and schedule of vitamin A administration to treat children with severe malnutrition and xerophthalmia do not appear to have been made.

At present the treatment given in some hospitals is to inject 100,000 I.U. of water miscible vitamin A each day for several days so that during the first week of treatment 500,000 I.U. or more is given. This may be followed by lower oral doses of an oil-solution of vitamin A. This schedule is not in accord with current recommendations. A healthy child of 2 to 3 years of age has about 50,000 I.U. of vitamin A in the liver; in the above treatment ten times that amount is given.

Recommendations: There is a need to establish in a few nutrition rehabilitation centers for children special research interests concerning corneal xerophthalmia. The aim of these would be to improve or confirm current treatment. The following suggestions are made.

1. The optimal treatment and dose schedule of vitamin A for the child receiving an otherwise adequate diet. WHO/U.S. AID currently recommends a treatment schedule of 100,000 I.U. water miscible vitamin A given intramuscularly immediately on diagnosis followed by 100,000 I.U. (oil) given orally on day two, and finally 100,000 to 200,000 I.U. (oil) given orally depending on the child's age prior to discharge. This schedule should be adopted as a basis and variations carefully introduced to ascertain if it can be improved.

2. The best ways to motivate and influence the mother to continue to provide a suitable diet to the child after return home needs further study.

3. Improved means of utilizing the nutrition rehabilitation center for educational purposes need research. The aim should always be to provide the needed vitamin A or carotenoid vitamin A precursor and protein in an acceptable, locally available diet which is cheap and available enough for the poor to obtain. In each geographic location, the best diet that is locally available must be formulated after investigation, account being taken of food taboos, prejudices and preferences.

4. Recommended laboratory investigations, such as those appearing elsewhere in this report, where appropriate, can be undertaken at appropriate rehabilitation centers.

Education

Prevention of avitaminosis A and its consequences is dependent upon wide understanding and practice of good nutrition among peoples throughout the developing world. Education is an essential component of any intervention procedure and all programs of intervention should provide opportunities for motivating people.

To achieve this goal, there is a major need for continuing research in educational methods conveying nutritional knowledge in terms that are meaningful to the cultural groups and in keeping with their resources.

Recommendation: Additional research is needed on the design, effectiveness, adaptation and evaluation of educational materials targeted for all levels including the physician, professional health worker, community and agricultural worker, formal educator and the general public.

Public Health

One obvious long-term solution to the problem of vitamin A deficiency and xerophthalmia is to improve the health of the population at risk. In all communities where the problem of vitamin A deficiency is recognized it is important that general public health measures be improved. The health services need to be able to detect the presence of xerophthalmia and vitamin A deficiency in the community; estimate, at least roughly, the prevalence of the condition; understand the epidemiology of xerophthalmia in different ecological zones; and have personnel able to undertake the diagnosis and treatment as well as establish programs of preventive xerophthalmia.

Xerophthalmia is most common among the poorest and most deprived families who are most difficult to reach and who least utilize the existing health and other services available.

Research into the public health aspects of xerophthalmia has tended to be neglected and this neglect should be rectified.

Recommendations:

1. Evaluation of the effects of public health measures on vitamin A nutritional status. This should not be a vitamin A study per se, but should be one component of the public health program. For example, using auxiliaries, it should be possible to ascertain the effect of a new system of health care delivery or a new feeding program on the vitamin A nutritional status of a community.

2. Studies of the interrelationship between both parasitic and infectious diseases and xerophthalmia should be undertaken. Such research should include the relationship of diseases like measles, ascariasis, gastroenteritis or protein-calorie malnutrition on the absorption and utilization of vitamin A and the conversion of carotene to vitamin A.

3. Research on the effect of various diseases on retinol-binding protein and the rate of vitamin A excretion in children should be expanded.

Agriculture

Since the long-term solution to vitamin A deficiencies in populations ultimately depends upon people consuming an adequate quantity of vitamin A or pro-vitamin A in their foods, together with an otherwise adequate diet, agriculture must supply food sources of vitamin A. It is therefore important that consideration be given to the production of commodities high in vitamin A and carotene (pro-vitamin A) or the use of indigenous sources of these nutrients. Several major possibilities exist in this area beyond educating the population to increase its consumption of dark green leafy vegetables and yellow fruits and vegetables. Within local areas there usually are several varieties of the typical commodities consumed in the diet. These often differ significantly in the level of bioavailable pro-vitamin A. Identification and promotion of the most beneficial one is a desirable step.

Recommendations:

1. The levels of pro-vitamin A in the locally grown vegetables and fruits should be ascertained and those most acceptable and having the highest concentrations should be selected for cultivation.

2. The development of any new varieties of the existing local foods with greatly increased pro-vitamin A should be encouraged.

3. Foods similar in taste, texture and appearance should be introduced, thus substituting closely akin foods containing a high pro-vitamin A concentration for those already being consumed in the community.

Combined Approaches

There is a tendency for countries and those designing programs to choose among several alternatives, such as the massive dose or fortification (nutrification), and not to give adequate consideration to combinations of programs that deal with vitamin A deficiency. It is also frequently the case that the problem of xerophthalmia is tackled independently of other nutritional and health problems. The Task Force believes that there is great merit in using several interventions simultaneously and in trying to solve the problem of vitamin A deficiency as part of a program aimed at preventing or controlling other health problems.

Recommendations:

1. Research in the combined approaches is appropriate in order to determine relative efficacy and cost-benefit ratio. For example, in one country three alternate strategies of control—the massive dose, fortification of MSG, and combined public health and horticulture—are being currently evaluated in four different areas, thus affording a comparison of the relative effectiveness of each type of program prior to the formulation of a national strategy for wider control. Such studies of alternate methods should be repeated in other countries using different strategies. But they should not exclude evaluation of combined strategies.

2. Nutrification or fortification programs in which both vitamin A and iron or other needed nutrients are added to a selected vehicle, in an attempt simultaneously to control both xerophthalmia and iron deficiency anemia, need to be supported.

OTHER RECOMMENDATIONS

Enzyme Changes in the Cornea

After many forms of injury to the cornea caused by burns, destructive proteolytic enzymes or other factors, collagenase develop. The ulcerating cornea of the xerophthalmic rat presents the same picture as it contains a more active collagenolytic system than the normal cornea. It is possible that the enzymes are released from the granulocytes which invade the cornea ahead of the capillaries. Some substances, such as EDTA and N-acetylcysteine, are known to inhibit these enzymes and can be used therapeutically on the burned cornea.

Recommendation: This already active field of research deserves further investigation directed toward possible immediate local treatment for the ulcerating cornea of xerophthalmia. The xerophthalmic rat, or other preferably larger animal, can provide a suitable model.

Conferences

The Research Task Force believes that it would be useful to convene a mini-conference of ten or fewer persons who would address themselves to the biochemical assessment of vitamin A nutritional status. Papers would be requested from participants prior to the meeting and these would be discussed. These papers and the proceedings of the meeting might be issued as an IVACG document and could be published as a series in some journal such as the American Journal of Clinical Nutrition. The mini-conference would also make recommendations for research in the area of the biochemical assessment of vitamin A nutritional status.

Regional or Care Centers for Vitamin A Research

The designation and support of regional centers in Asia, Africa and Central and South America are recommended. These would have laboratory facilities capable of making the necessary biochemical determinations for surveys in those countries in the region that are not able to undertake these determinations themselves. These centers would also be able to provide assistance for the standardization of methodology, for training of personnel in the region and to undertake or assist with research. Library facilities for each regional center would be desirable. Places having resources which might serve as regional centers include: in Asia, the Nutrition Research and Development Center at Bogor in Indonesia and the Nutrition Research Center at Hyderabad in India; in Latin America, at INCAP in Guatemala; and in the Middle East, at NAMRU-3 in Cairo. No suitable site is currently available in Africa south of the Sahara, but one should be established.

Reference or Information Center

It is recommended that IVACG establish a reference or information center. This would serve as a depository for IVACG materials. Fairly modest facilities would be required but should include one room for housing documents relating to vitamin A deficiency and xerophthalmia, as well as a librarian and supporting staff whose work would be supervised by a senior staff member or person involved in the work of IVACG. Such a reference or documentation center could be set up by contract with AID or some other donor agency. It might be established in one of the existing organizations or agency which have membership in IVACG or in a suitable university. The objective would be to have in one place: (a) a reference library relevant to the needs of IVACG members and organizations; (b) an up-to-date documentation of research of relevance to IVACG; (c) details of the status of prevalence surveys in developing countries; (d) a system which could retrieve, copy and dispatch to IVACG members and workers in the developing countries materials related to vitamin A deficiency.

This recommendation is made by the Research Task Force because we believe that such a reference center would be of particular value in promoting applied research in the area of vitamin A deficiency.

Consideration should be given to housing the Secretariat of IVACG in the same location as the reference center.

V.
RECOMMENDATIONS OF IVACG CONCERNING RESEARCH AND DEVELOPMENT NEEDS

March 23-25, 1976
Port-au-Prince, Haiti

RECOMMENDATIONS

1. A permanent Secretariat should be set up as soon as possible in conjunction with an information clearing house on vitamin A. The function of the Secretariat would be to receive and distribute information on vitamin A, to schedule and develop reports derived from discussions of IVACG or subcommittees and to maintain liaison with other groups interested in vitamin A and donor agencies.

2. A reference laboratory for vitamin A analysis should be established. This laboratory would not have to be created *de novo* but should be part of a nutritional facility having expertise in vitamin A analysis. It could, on occasion, be utilized for analysis of samples derived from assessment programs, but more importantly, it would serve to standardize the analytical procedures and programs of analysis of cooperating laboratories.

3. A roster of individuals having expertise in different areas of vitamin A programming should be compiled. It is recognized that it may be necessary to train additional personnel, especially in the clinical aspects of vitamin A deficiency, as part of the development of this bank of talent.

4. Project(s) should be established to develop better methodology for the determination of vitamin A precursors, particularly in food-as-consumed. This would also involve the determination of provitamin A in various agricultural commodities now available in local areas.

5. Development of a project to standardize methods for collecting and storing tissues in preparation for vitamin A assay. A retinol-binding investigation should determine whether measurement of retinol and RBP and/or vitamin A:RBP ratios would be helpful in determining the vitamin A nutriture of a population. Support should be considered for studies better to define and quantitate the excreted metabolities of vitamin A to determine whether or not they may serve as a useful basis for measuring vitamin A.

6. Work should be supported on the physiology of vision to determine whether measurements of visual phenomena such as night blindness may be useful in early detection of vitamin A deficiency.

7. Research and utilization of staining techniques to determine xerosis conjunctivae should be supported.

8. Work should be supported to define whether taste impairment and color discrimination result from vitamin A deficiency and, if so, whether the impairments may be useful symptoms of human vitamin A deficiency.

9. Additional studies should be supported to determine which foods for various populations are suitable for nutrification with vitamin A. Vitamin A preparations to be added to foods at home should be field tested.

10. Because of the concern about the efficacy of intermittent high level dosing of vitamin A, further research is justified to provide a better understanding of the absorption, storage, transportation and excretion of vitamin A supplied in this manner.

11. All intervention programs should have a built-in evaluation mechanism at the outset of planning. To achieve this, it is recommended that this evaluation expertise, insofar as possible, be drawn from national resources. Duplications of evaluations already tested should be avoided.

12. It is recommended that two distinct phases of evaluation processes be identified: an intensive initial evaluation and an ongoing monitoring process. No program should be undertaken which does not incorporate some informative degree of evaluation. Minimal, low cost, critical indicators should be used to evaluate the effectiveness of programs.

13. Recognizing the impracticality of building regional research centers devoted entirely to vitamin A within the existing nutritional framework, it is recommended that encouragement be given to establishing groups or sections within existing institutes or centers to deal specifically with the problem of vitamin A nutriture.

Participants in the IVACG meeting held March 23-25, 1976, Port-au-Prince, Haiti, at which time these guidelines were reviewed and approved.

Attendees:

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Clinton O. Chichester, The Nutrition Foundation, U.S.A.
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