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EVALUATION OF PROGRAMS TO CONTROL VITAMIN A DEFICIENCY*

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The International Vitamin A Consultative Group (IVACG) has recently published the "Guidelines for the Eradication of Vitamin A Deficiency and Xerophthalmia."[1] Because of the simple definition of evaluation used by this group, we cannot do better than to quote from their publication: "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."

To this we may add that any approach to evaluation must have three distinct components, which are complementary but relatively independent: (1) Evaluation of the operation. In the case of programs designed to convey a desired nutrient to a target population, this could be called the evaluation of the delivery system. (2) Evaluation of the biological effectiveness; that is, to what extent the properly done intervention modifies the undesirable preexisting situation. (3) Cost of the intervention, which expressed in combination with (2) gives the "cost-effectiveness" or "cost-benefit ratio."

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Within this general conceptual framework we shall, in this paper, analyze some intervention programs recently developed to correct vitamin A deficiency, and particularly the efforts that have been made to evaluate them.

Vitamin A deficiency has long been recognized as one of the serious and most generalized nutritional problems affecting the vast majority of the populations in the underdeveloped world. It was not until recently, however, that the emphasis changed from simply describing the problem, as well as its magnitude and irreparable consequences to health, to emphasis on urgent measures to correct this undesirable situation. In a recent report of a joint WHO/USAID Meeting[2] it was recognized that vitamin A deficiency continues as a highly prevalent nutritional problem, ". . . even though scientific knowledge and technological skills could now markedly reduce its prevalence at a relatively modest cost." In this same report WHO stated its intention to give high priorities to action programs to eliminate vitamin A deficiency.

It is quite obvious that, in theory at least, the number of different intervention approaches from which to select is not small. For example, IVACG in its 1976 report[1] lists as "available strategies" the following: nutrification of foods; massive dosing; horticultural approaches; nutrition education; public health measures; socioeconomic approaches; and combined interventions. Of these seven, however, massive dosing and nutrification of foods can be considered direct interventions with the potential for rapid implementation that quickly leads to measurable results. It is for that rea-

son that we will concentrate our attention on these two proposed strategies.

This does not mean that the other more general and less direct approaches are to be disregarded, but the vitamin A deficiency problem is so severe, and its sequelae so dramatic and damaging, that efforts to implement short-term measures are definitely in order.

MASSIVE DOSING

Due credit has to be given to the group of investigators at the National Institute of Nutrition of Hyderabad, India, for development of this approach. The stimulus to this group obviously came from the abundant evidence that vitamin A deficiency in India has resulted in a very large number of people, particularly children, who are left permanently blind. The principle behind this intervention has been described elsewhere.[3] Briefly stated it recognizes the impossibility of changing the overall dietary patterns of the affected populations rapidly enough to result in any foreseeable improvement. From the biological point of view, it is based on the fact that vitamin A in the form of retinyl esters is stored in the liver when given in large quantities, and that these stores, depending on their magnitude, can supply the needed vitamin A to the tissues for varied periods of time, extending to as long as 2 to 3 years in an adult and from 4 to 6 months in a small child. On those bases the investigators proposed and tested the oral administration of a large dose of retinyl palmitate in oil which was to be administered periodically to the specific most vulnerable groups of the population. In India, as is the case in most of the world, the preschool child is clearly the target group of a program like this. It is in this group that the peak of active clinical manifestations of vitamin A deficiency are observed and in whom the alterations leading to permanent damage of the eye begin.

After several years of research during the last decade, testing different massive doses as well as different time intervals for their administration, the Hyderabad group recommended a dose of 200,000 I.U. of vitamin A orally once in 6 months. The liver reserves built up in this manner were shown to raise serum levels and maintain them higher than the basal values for most, if not all, the interval of 6 months.

The Government of India officially adopted this approach and started the National Program for the Prevention of Blindness, which has been in operation for the last 6 years. The initiation of this program was preceded by pilot studies conducted by the National Institute of Nutrition in Hyderabad that showed success in decreasing the incidence of vitamin A deficiency in preschool children ages 1 to 4 years. The program is carried out under the joint responsibility of the State Nutrition Officer and the State Family Planning Officer. It is implemented by the Medical Officer of the Primary Health Center, and the actual distribution of the vitamin A capsules is done by the auxiliary nurse midwife or by the health visitor through a system of house-to-house visits.

Efforts have been made to expand progressively the coverage of the program. For example, in 1972, the number of children involved was 2.6 million; in 1973, it was 4 million; in 1974, the program was officially implemented in 14 states and the number of children reached was 6 million. The last figure reported from the National Institute of Nutrition[1] was a target number of 13 million children at the end of 1976.

How successful has this program been? We will try to answer this question in the light of the three distinct evaluation phases described before:

Evaluation of the delivery system It is obvious that one very important question in an extensive program such as this is whether all the vitamin A supplied reaches its final target at the individual level. In this particular case it is assumed that if 13 million children were the target group, 200,000 I.U. of vitamin A would be swallowed by each one of them every 6 months. However, as stated by Vinodini Reddy,[4] "these figures are based on the doses of vitamin A supplied to the different States but it is difficult to say how many children have actually received the dose because complete records have not been obtained from all the States." Therefore, for the National Program at large, evaluation of the de-

livery system has to be considered inadequate.

In one of the State programs (Karnataka State), however, it is apparent that a more concentrated and complete effort to evaluate the program has been conducted. This evaluation was intended to investigate the actual coverage of beneficiaries, the community response and the clinical impact. Through records maintained by the Auxiliary Nurse Midwives it was determined that the coverage was about 90% for the first dose and 75% for the second. A cross-checking system was applied by interviewing the parents and other members of the community to validate further the data obtained. In the opinion of the investigator the response of the community to the program was favorable. It may be of interest to meditate on a comment by Doctor Reddy regarding the fact that at the onset of the program there was misapprehension about the program because the bottles of vitamin A had on the label the Family Planning symbol, which led many of the members of the communities to think that the vitamin A was intended to sterilize the children. No explanation is advanced as to the reason for the decrease from 90% to 75% from the first to the second distribution period. There is evidence from other efforts of massive dose distribution in other areas of Asia that it is extremely difficult to maintain the initial high levels of coverage, which may be one of the points of concern regarding this type of intervention since it requires the willingness of the population to participate.

Biological effectiveness The evaluation of the clinical impact was possible because of the availability of baseline data regarding the incidence of vitamin A deficiency ocular signs among the target population. Table 1, taken directly from the report by Reddy,[4] indicates a "substantial" reduction in the prevalence of vitamin A deficiency. Taking together the two main ocular signs selected by the investigator, Bitot's spots and conjunctival xerosis, a decrease in prevalence from 7.4% before the program to 3% after two doses of vitamin A is reported.

In addition to the evaluation reported in Karnataka, a similar evaluation survey carried out in Kerala State concluded that the number of children having eye signs of vitamin A deficiency dropped from 6% before the program to 1.3% after the second dose.

It is the opinion of the Indian investigators that from the observations discussed it can be concluded that the massive dose program is an administratively feasible public health measure within the existing infrastructure of health services and that it is effective in reducing morbidity due to hypovitaminosis A.

In our opinion this assertion is too general and may give the impression that the application of the massive dose program is administered more easily than it really is. In fact, the investigators responsible go further to state that "the program has not achieved the same success in other states due to administrative reasons. The problems encountered in some of the areas are lack of personnel, inadequate coordination, poor record keeping and the lack of built-in evaluation."[4]

Cost To our knowledge, no evaluation of the total cost of a massive dose program has been reported. Reddy[4] reports that the cost of the vitamin A dose per child per year is about 6 US cents, but the cost of the distribution of the capsule from the base of operation to the mouth of the child is not estimated. Considering the large number of personnel involved and the time and effort involved in a house-to-house distribution system, it is reasonable to suppose that the actual total cost is much higher.

It is hoped that in the near future a complete analysis of this type of program is made available, particularly to ascertain its administrative feasibility and its potential to maintain a high and stable level of coverage through the years. These are as yet unanswered questions.

NUTRIFICATION OF FOOD VEHICLE WITH VITAMIN A

Implementation At the Western Hemisphere Nutrition Congress III, Arroyave[5] discussed nutrification of food and analyzed the reasons for the selection of sugar as the most promising carrier of vitamin A to the popula-

Table 1
Percentage Prevalence of Deficiency Signs Before and After the Administration of Vitamin A (from Reddy[4])
(Karnataka State)

Age Group (years)	Before vitamin A was administered				After two doses of vitamin A			
	Number	Conjunctival xerosis	Bitot's spots	Total vitamin A deficiency	Number	Conjunctival xerosis	Bitot's spots	Total vitamin A deficiency
1-3	947	2.6	1.3	3.9	567	0.7	0.2	0.9
3-5	633	6.5	6.2	12.7	573	3.8	1.2	5.0
1-5	1580	4.2	3.2	7.4	1140	2.3	0.7	3.0

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tions of Central America. On that occasion, it was reported that the development of a process that made possible the addition of water-dispersible vitamin A palmitate to sugar was taking place at the Institute of Nutrition of Central America and Panama. The final comments in that paper read: "From what has been described, it appears that no major problems will be encountered in the implementation of this important public health measure at the national or regional level. In two member countries of INCAP, arrangements are well advanced to take this pioneering step. Specifically, the form of financing the process is being discussed at the government level with the participation of the sugar manufacturing sector and INCAP. Furthermore, a law is being proposed which will dictate the specifications of the process, of the control system and of the mechanism of enforcement."

A perusal of this literature leads one to ask at this time the question: Have we advanced significantly since 1971? The research on the development of the process of sugar fortification with vitamin A was completed soon after that time, yielding a process through which all the sugar produced in a country can be fortified with a water dispersible form of retinol palmitate utilizing a premix that ensures that the vitamin does not segregate from the sugar.[6,7] This process has been proposed by INCAP as a measure to attack the problem of hypovitaminosis A at the national level, until other more permanent measures consequent to socioeconomic development become feasible. Sugar fortification has been legally approved as a compulsory program in four Central American countries, Costa Rica, Guatemala, Panama and Honduras. The first three of them have already implemented the measure and Honduras is ready to begin with sugar fortification at the national level in November 1977.

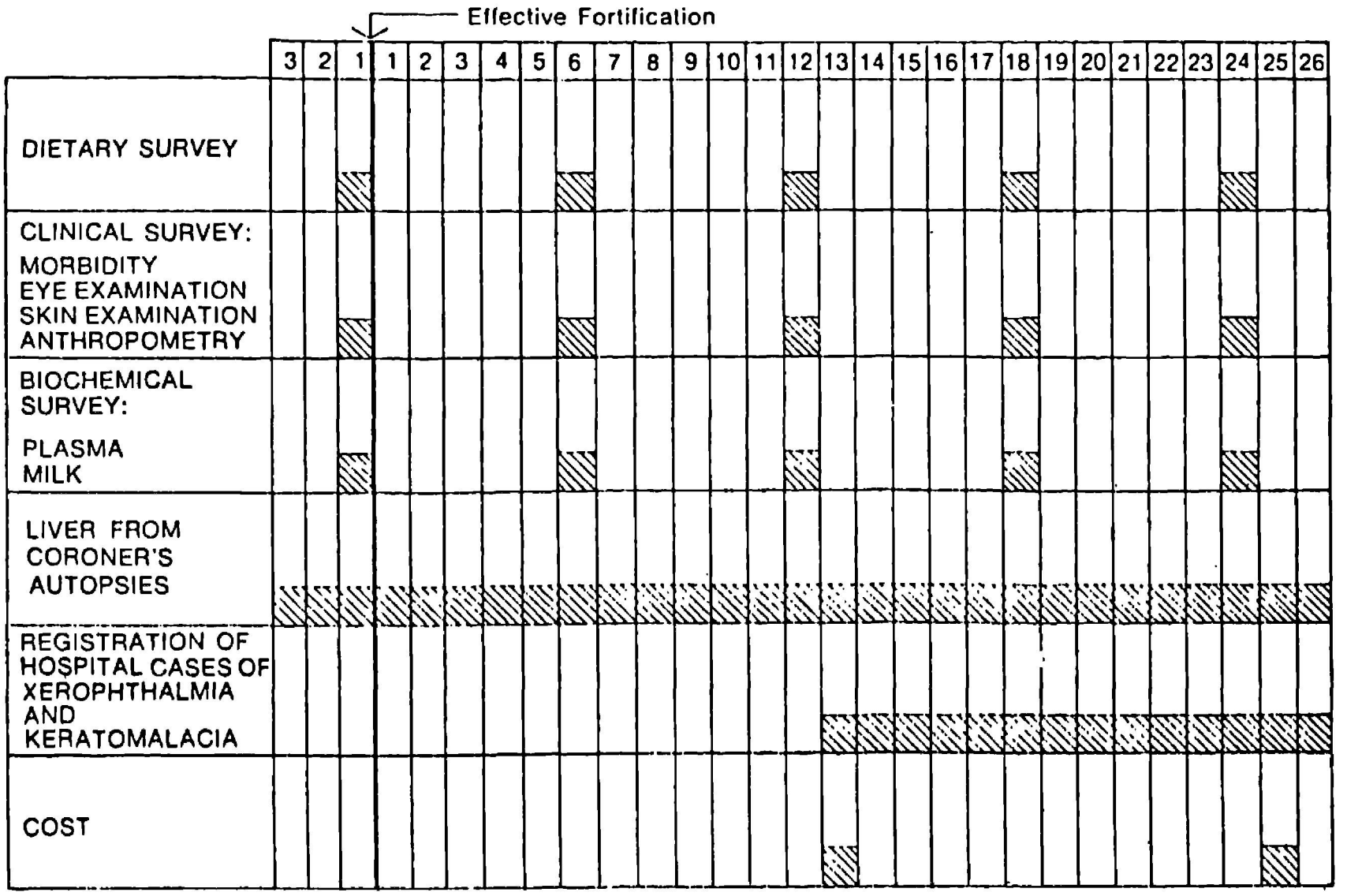
EVALUATION OF THE PROGRAM

1. Basis and plan The evaluation study to be described is based on the premise that the application of a public health intervention program without adequate built-in evaluation is wasteful, since the potential of the program for application in similar situations elsewhere would be undetermined. In the particular case of fortification of sugar with vitamin A, this is of utmost importance; this measure proposed to solve the problem of hypovitaminosis A has never before been applied anywhere in the world.

Most population groups in the underdeveloped world are, as mentioned before, suffering from vitamin A deficiency, and it would be expected that if the experience in Central America with sugar fortification is successful, that is, if the program is proved effective, many countries would be interested in considering its implementation.

Although vitamin A fortification of sugar has demonstrated effectiveness in the laboratory and in small population groups, its effectiveness and cost have to be assessed at the national or large regional level. To this end, an evaluation program was designed. The objectives of this project are to evaluate: (a) the delivery system of the fortified sugar; (b)

Figure 1
Evaluation of Sugar Fortification with Vitamin A
Calendar of Operations
Guatemala



the biological effectiveness; and (c) the cost of the intervention.

The evaluation of the program began in Guatemala in September 1975, immediately before the initiation of fortification at the national level. The first phase consisted of a nutrition survey with the specific objective of obtaining baseline information on the nutritional status of the population with respect to vitamin A. In addition, data on the consumption of natural food sources of this vitamin were also collected.

The overall study included: (a) a dietary survey, to determine the daily intake of sugar and of natural sources of carotenes and preformed vitamin A; (b) a clinical survey which included skin examination in all persons in the study sample; and in preschool children, general morbidity, eye signs of vitamin A deficiency and anthropometric measurements; (c) biochemical investigation to determine the blood serum vitamin A levels in children of preschool age, and the vitamin A content of human milk from all lactating women present in the sample of population.

This baseline study was concluded in November 1975. According to the evaluation plan, four additional nutritional surveys were to follow the initial one at intervals of six months during the years 1976 and 1977. The purpose of this experimental design is to determine the changes in the parameters being measured which will reveal the extent of the biological effectiveness of the fortification program and the effects that seasonal variation may have (Figure 1).

Three of these follow-up surveys have been completed to date. The first one during April-May 1976, the second, during October-November 1976 and the third, during April-May 1977. One additional survey will be carried out at the end of the rainy season in 1977. The studies described above are being carried out in 12 rural communities of Guatemala, with populations between 1000-2000 inhabitants. These populations were selected at ran-

Table 2
Evaluation of Sugar Fortification with Vitamin A.
Numbers of Dietary Questionnaires and Families Having Clinical Examination;
Numbers of Blood and Milk Samples Obtained
Guatemala 1975-1977

Period of survey	Families		Samples obtained	
	Dietary questionnaires	Clinical examination	Blood	Milk
Baseline Oct-Nov 75	360	253	537	283
1st. follow-up Apr-May 76	360	269	587	313
2nd. follow-up Oct-Nov 76	360	253	647	236
3rd. follow-up Apr-May 77	360	248	655	281

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dom by statistical methods and are representative of the principal rural ecological areas of the country. Within each community 30 families were randomly selected. It is important to emphasize that *the main objective of the program is to increase the intake of vitamin A to approach or, even better, to reach 100% adequacy for preschool children when compared with recommended intakes, and through this improved intake to raise the blood serum levels among the population at large, increasing thereby the supply of retinol to the tissues.* This contrasts with the primary clinical objective of the massive-dosing program where the evaluation criterion is a reduction in the prevalence of eye signs of deficiency. A thorough discussion of our point of view regarding this question has been published elsewhere[4] and is included as an appendix to this paper.

The critical indicator chosen to define the size of the sample is, in our program, the proportion of subjects with low levels of serum vitamin A. This biochemical indicator is probably the most effective and sensitive for detecting, at the population level, the changes that may result from the generalized consumption of sugar fortified with vitamin A. In this connection, results from the nutritional surveys of Central America and Panama[9] show that in Guatemala, the prevalence of low serum vitamin A values (less than 20 μg/100 ml) in children of preschool age oscillated around 25% and, on this basis, a sample of 300 children of preschool age will permit the identification of a net change of 10% units in the baseline prevalence of low serum vitamin A levels.

2. Results and discussion Table 2 presents the numbers of dietary questionnaires, families attending the clinical examination, and samples of blood and milk obtained in the surveys. It illustrates a very satisfactory degree of community response. The numbers of observations are higher than the minimum required by statistical criteria.

a. Delivery system Regarding the delivery system, the important questions are:

- Is the sugar being fortified and at what level of efficiency?
- Is it reaching the target population?
- Is it being consumed and to what extent?

A system of supervision and control has been established at each sugar factory where a record is kept daily of the amount of sugar produced and of the vitamin A premix used. From those data a fortification ratio at the level of the factory is obtained.[10] Samples are taken for quantitative determination of retinol.

In addition, samples of sugar are periodically collected from the 12 villages selected for study, both from the village stores and from the households, and the level of fortification is determined by analysis. A rapid colorimetric method has been developed by INCAP for the estimation of vitamin A in sugar samples.[10] The daily intake of sugar is being measured by periodic dietary surveys, conducted by the dietary team which visits the

Table 3
Sugar Fortification with Vitamin A
Guatemala, 1975-1976

Sugar production (qq)*	Fortified sugar (qq)	Percentage (%)	Estimated level of fortification (μg/g)
4,197,867	3,137,317	75	13

*(1qq = 100 pounds)

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communities the week before the clinical-biochemical team.

Table 3 illustrates the type of records obtained from the sugar factories. The proportion of sugar that was fortified reached 75%. The non-fortified sugar is, by law, supposed to serve only for use in industrial processes where the vitamin A is known to be destroyed, or unnecessary.[11] However, we have found that some of this non-fortified product is reaching the population for direct table-use. In the second follow-up survey for example, the average percent of household samples of sugar found to be fortified was 70%. Measures are being taken to correct this irregularity.

Table 4 shows data collected in 1965[9] on the consumption of white sugar and *panela* (crude-caked sugar not fortified) by preschool children. The information from the present surveys is still being analyzed. Including all family members the daily per capita average consumption of white sugar for 1975 and 1976 was 35 and 34 grams respectively. It is interesting that in 1965 this latter figure was 36 grams, showing the stability of the dietary characteristics of this rural population.

Table 4
Control of Hypovitaminosis in
Central America. Sugar Consumption by Rural Preschool Children*
(Guatemala 1965)

Age group (years)	N	White sugar (g/child/day)	Panela
1	38	28	6
2	43	22	9
3	35	19	11
4 y 5	14	20	13

*INCAP/OIR Survey, 1965.

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b. Biological effectiveness At the start of the discussion of this point we would like to re-emphasize the nutritional nature and clear nutritional objective of sugar fortification with vitamin A. Therefore, basic to the selection of the intervention and to the approach to evaluation was the consideration of the evidence that the vitamin A intake of the target population from natural food sources was unacceptably deficient (shown in Table 5). In addition, and in agreement with this fact, a high prevalence of undesirably low values of retinol in serum from preschool children and in mother's milk samples was demonstrated in the population. Therefore, the principal indicators chosen to detect and measure the impact of the program were blood serum levels of preschool children and levels of retinol in mother's milk. The justification for the decision to study blood of only preschool children is based on the fact that they constitute the most vulnerable age group and also consume the lowest amounts of sugar among the family. Consequently, if a positive effect of the fortification is shown for this age group, the unavoidable conclusion has to be that older children and adults are also benefited and perhaps even more.

The concentration of vitamin A in blood serum has proved very useful as an indicator of the adequacy of nutritional status in regard to vitamin A. The significance of this parameter to define the population at risk has been emphasized by Arroyave.[12] Data obtained from the Sheffield experiment,[13] confirmed by epidemiological observations, were interpreted by the Group of Experts of the ICNND[11] to elaborate their guide for the interpretation of blood vitamin A levels shown below:

Table 5
Evaluation of Sugar Fortification with Vitamin A.
Level of Adequacy of Vitamin A in Diet—Baseline Survey*
(No. of families 357)

% adequacy	25<	25-49	50-74	75-99	100>
% families	89.6	8.5	1.1	—	0.8

*Oct-Nov/75

Plasma Vitamin A (μg/100 ml)			
Deficient	Low	Acceptable	High
<10	10-19	20-49	≥50

More recently Sauberlich et al[15] have concluded experiments in human adults that encourage them to suggest the level of 30 μg/100 ml of serum (instead of 20 μg) as the cut-off point to separate low from acceptable values, since their studies show that "30 μg/100 ml would be necessary to ensure modest body stores of the vitamin." The data obtained on the preschool children in the rural sample are being analyzed in terms of their distribution. A basic criterion to judge the effectiveness of the program is the shift of the distribution curve of serum retinol values. This approach is indicated by IVACG.[1]

The study of human milk is important because of two facts. One, that in the type of population under study, infants are breast-fed with insignificant supplementary foods for an average of 1½ years and, therefore, we wanted to know the extent to which the program would affect the vitamin A intake of the breast-fed babies. Second, that our previous studies have shown a high prevalence of very low retinol concentrations in milk in these areas; these levels increase significantly during the consumption of vitamin A fortified sugar as part of the regular dietaries.[16]

Figure 2 presents the distribution of serum values for each of the follow-up surveys compared with the baseline. The data from the first follow-up survey showed a slight improvement. The difference, although not significant, was encouraging. In fact, there were two circumstances that had led us not to expect a very marked impact: (1) at the time this survey was carried out, fortification had been in operation for only four months; and (2) April-May corresponds with the end of the dry season, and it was during this period of the year that previous INCAP studies had shown the lowest serum vitamin A levels, in contrast with the end of the rainy season (November).

The second follow-up survey gave higher values with a highly significant different distribution ($P < 0.001$). Both sets of data, baseline and second follow-up, were collected during October-November, end of the rainy season of 1975 and 1976 respectively. The values obtained during the third follow-up survey, although somewhat lower than those of the second are still significantly ($P < 0.001$) higher than the baseline, despite the fact that the baseline coincided with the end of the rainy season and the third follow-up survey was at the end of the dry season.

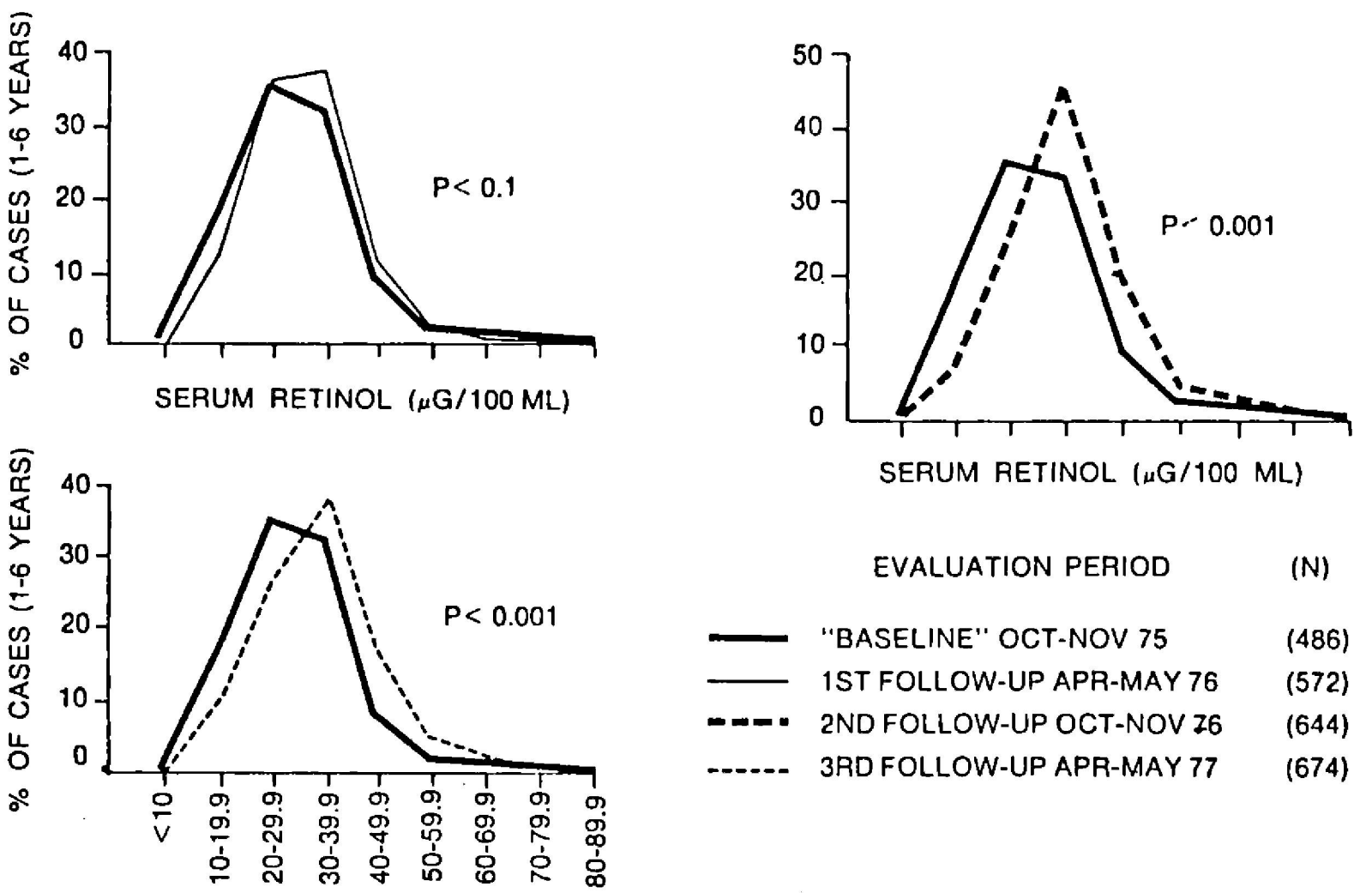
Figure 3 presents the distribution curves of breast milk retinol values. As in the case of serum levels, a clear shift can be observed from the baseline survey, which becomes highly significant at the second follow-up survey ($P < 0.001$) and increases further in the third follow-up survey.

The fourth follow-up survey is scheduled for October-November 1977.

A number of additional studies were carried out in a longitudinal manner during the two-year observation period reported herein. These included clinical observations of eye lesions and the analysis of vitamin A in liver samples collected at the morgue in Guatemala City, from legal autopsies performed in accidental deaths. These data are still being analyzed.

c. Cost The analysis of the cost of the program will be necessary for the determination of its cost-benefit ratio. The main component of program cost is the vitamin A prep-

Figure 2
Evaluation of Sugar Fortification with Vitamin A
Change Observed in Blood Serum Retinol Concentrations in Pre-School Children
Guatemala



aration, which amounts to over 95% of total cost. Taking this item alone the cost for the sugar manufacturing season 1976-1977 was $475.000 (US). If this figure is expressed on *per capita* basis for Guatemala it is estimated that it costs at present around 8 cents per year per inhabitant.

The impact of this cost on the sugar prices is considered negligible; in fact it represents about $0.0014 of the $0.11 per pound selling price. The other components of the total cost, as mentioned before, amount to 5% or less, and represent the preparation of the premix, its transportation to the factories, and the supervision and control of the process. It is to be emphasized that the application of the process does not require any additional personnel in the factories. A complete analysis of cost will be reported at the end of the evaluation program after December 31, 1977.

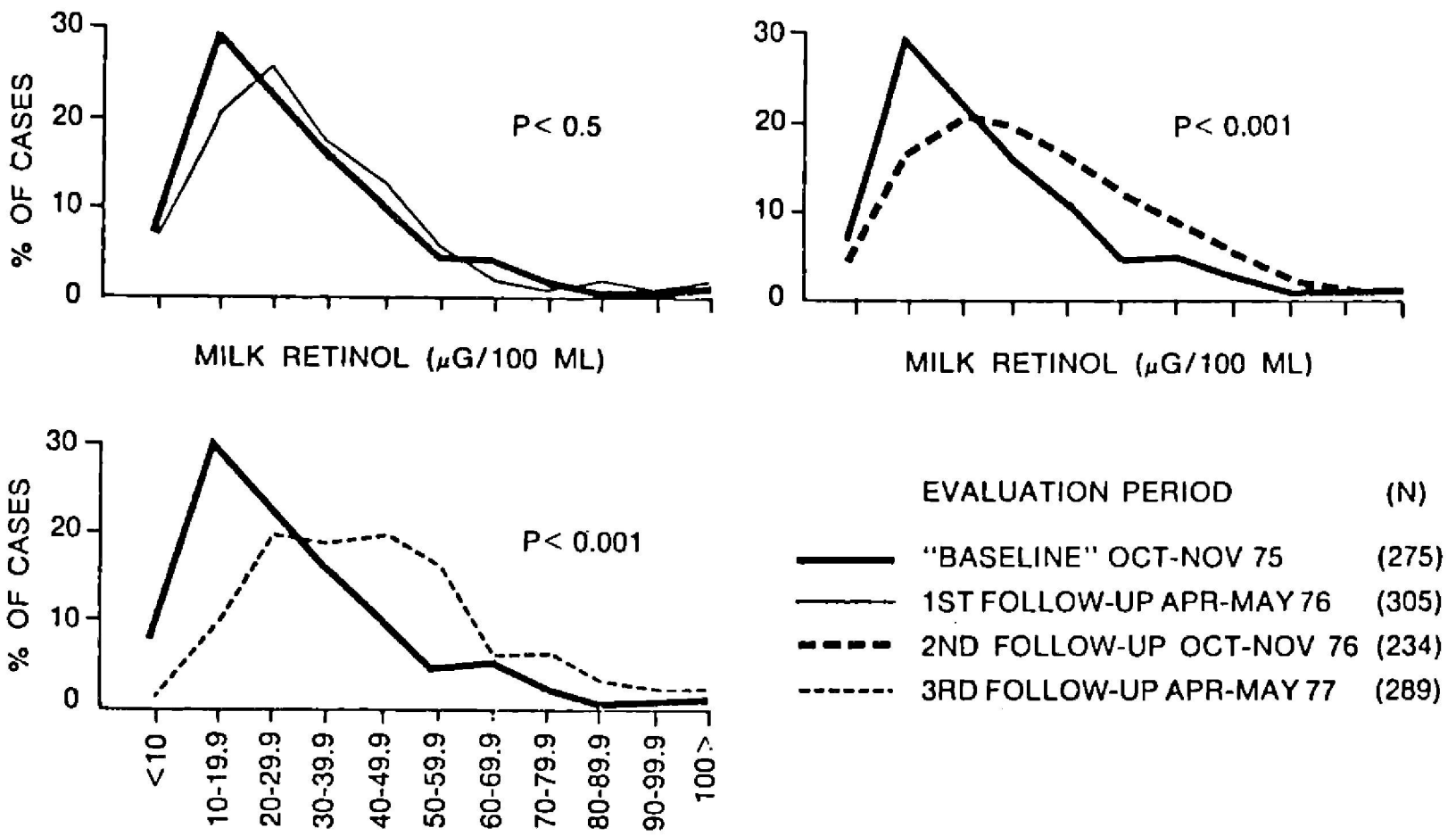
In accordance with the objectives of the intervention, *benefit* will be expressed in terms of the number of persons who, before the program, were in an undesirable situation in relation to the indicator chosen, and who were shifted by the program to an acceptable situation.

3. Conclusion The data available to date and presented here indicate a marked improvement in the biochemical indicators discussed. From the nutritional point of view, therefore, it can be concluded that vitamin A in sugar is producing a clear impact on the vitamin A status of the target population.

APPENDIX[5]

"Keratomalacia is the last event in the chain of clinical manifestations of vitamin A deficiency. Cases of this condition occur in children who are basically protein-calorie malnourished and have also a low vitamin A nutrition, in whom the severe corneal lesion is usually precipitated by an infection. As is the experience in several parts of the underdeveloped world children who develop this condition either get hospitalized or die. For the reasons outlined, cross-sectional prevalence studies of keratomalacia among samples of ambulatory population do not give a true picture of the damage caused by vitamin A

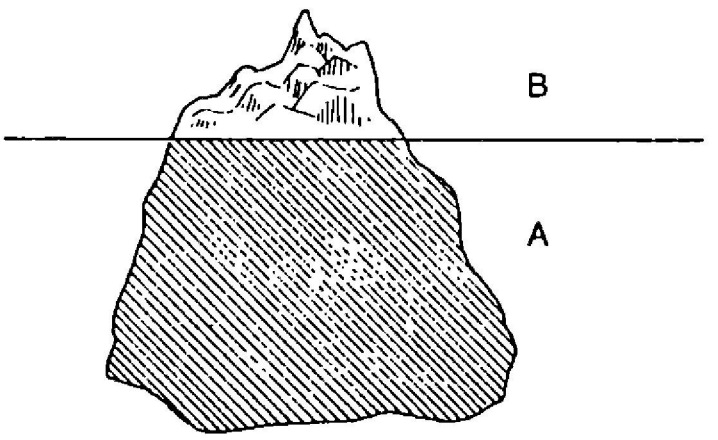
Figure 3
Evaluation of Sugar Fortification with Vitamin A
Changes Observed in Retinol Concentration of Human Milk
Guatemala



deficiency, including that of the eye. It is wrong to conclude that there is no serious vitamin A deficiency problem from results obtained through that approach which give low prevalence figures. True incidence cannot be derived from those data.

"The case of vitamin A is very similar to that of protein-calorie malnutrition (PCM). The severe forms of PCM (kwashiorkor and marasmus) are found rarely among population samples in our countries. The pediatric wards are abundant in them. Numerous studies leave no doubt that PCM is generalized in the same populations, with all its undesirable consequences for the individual and the society. The iceberg image best illustrates this.

"This principle has been taken into consideration in the design of the Evaluation System of the fortification of sugar with Vitamin A at the National Level."



B. Only part that can be seen: Kwashiorkor-Keratomalacia

A. 'Hidden' portion of problem: chronic sub-clinical deficiency; biochemical and physiological damage. Population at risk of passing easily from A to B.

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