| BIBLIOGRAPHIC DATA SHEET | 1. CONTROL NUMBER PN-AAJ-738 | 2. SUBJECT CLASSIFICATION (695) NA00-0000-G356 |
|---|---|---|

3. TITLE AND SUBTITLE (240)

Evaluation of sugar fortification with Vitamin A at the national level

4. PERSONAL AUTHORS (100)

Arroyave, Guillermo; Aguilar, J.R.; Flores, Marina; Guzman, M.A.

5. CORPORATE AUTHORS (101)

Pan Am. Health Organization

| 6. DOCUMENT DATE (110) | 7. NUMBER OF PAGES (120) | 8. ARC NUMBER (170) |
|---|---|---|
| 1979 | 82p. | GT641.1.A773 |

9. REFERENCE ORGANIZATION (130)

PAHO

10. SUPPLEMENTARY NOTES (500)

11. ABSTRACT (950)

12. DESCRIPTORS (920)

Vitamin A
Sugars
Guatemala
Nutritional deficiencies
Program evaluation
Nutrition
Health
Vitamin deficiencies
Diets

13. PROJECT NUMBER (150)

14. CONTRACT NO.(140)

AID/ta-C-1225

15. CONTRACT TYPE (140)

16. TYPE OF DOCUMENT (160)

AID 590-7 (10-79)

GT
6411
A773

PN-AAJ-738

Scientific Publication No. 384

# Evaluation of Sugar Fortification with Vitamin A at the National Level

Guillermo Arroyave
Juan R. Aguilar
Marina Flores
Miguel A. Guzmán

of the

Institute of Nutrition
of Central America and Panama

1979

# EVALUATION OF SUGAR FORTIFICATION WITH VITAMIN A AT THE NATIONAL LEVEL

Guillermo Arroyave
Juan R. Aguilar
Marina Flores
Miguel A. Guzmán

of the

Institute of Nutrition of
Central America and Panama

Scientific Publication 381

PAN AMERICAN HEALTH ORGANIZATION
Pan American Sanitary Bureau, Regional Office of the
WORLD HEALTH ORGANIZATION
525 Twenty-third Street, N.W.
Washington, D.C. 20037

1979

**Issued in Spanish (1979) as:**
***Evaluación del programa nacional de fortificación de azúcar con vitamina A***

The evaluation of the program of fortification of sugar with vitamin A in Guatemala was carried out under grant No. AID ta C 1225 from the Agency for International Development of the United States of America.

ISBN 92 75 11384 X

Pan American Health Organization 1979

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**Acknowledgments**

The present study was made possible by the active support and cooperation of many agencies. Special appreciation is expressed to:

*The Ministries of Health, Education, and Defense of Guatemala*

*The National Association of Sugar Manufacturers of Guatemala, Ingenio El Salto, Guatemala*

*The National Committee for the Blind and Deaf of Guatemala*

*The Association of Sugar Technologists of Guatemala, particularly the chief engineers of the sugar factories*

Deepest recognition and gratefulness are acknowledged to the 12 communities that participated in this study, particularly to their local authorities and agencies, the families and their children, without whom the objectives of this study could not have been attained.

# Introduction

## BASIC CONSIDERATIONS: THE PROBLEM

Epidemiologic investigations carried out by INCAP in the countries of Central America and Panama during the nutrition surveys of 1965-1967 (*1*) confirmed the existence of a severe and widespread problem of hypovitaminosis A in the population.

This was first made evident by the distribution of families by per cent of vitamin A intake, as shown in Table 1. Even in the best of the cases, over 40 per cent of the families surveyed had intakes of less than one fourth of the recommended daily allowances (2). In El Salvador nearly 70 per cent of the families fell in this alarming category. This situation of vitamin A deficiency was confirmed by the data on blood serum retinol, as indicated in Table 2 which shows the number of children under 15 years of age with vitamin A serum values below 20 μg/100 ml, a level that is considered undesirably low (3). It could therefore be estimated that in 1965-1967 around 1.5 million children below 15 years of age were affected with hypovitaminosis A. If the minimum acceptable level suggested by Sauberlich et al. (*4*), i.e., less than 30 μg/100 ml, is taken, the number of affected children would have been much higher. In any case, the prevalence, as defined (< 20 μg/100 ml), averaged 31 per cent in the 0-4 year olds for the six countries, reaching 43 per cent in El Salvador.

In view of this, the Institute of Nutrition of Central America and Panama (INCAP)

**Table 1. Distribution of families by percent adequacy of vitamin A intake.[1]**

| Country | Number of families surveyed | Level of adequacy of vitamin A in diet (percent of adequacy) | | | | |
|---|---|---|---|---|---|---|
| | | <25 | 25-49 | 50-74 | 75-99 | ≥100 |
| | | - Percent of families at each level - | | | | |
| Guatemala | 200 | 45 | 22 | 10 | 6 | 17 |
| El Salvador | 278 | 69 | 19 | 7 | 3 | 2 |
| Honduras | 323 | 57 | 26 | 9 | 2 | 6 |
| Nicaragua | 331 | 45 | 23 | 13 | 8 | 11 |
| Costa Rica | 414 | 44 | 26 | 11 | 7 | 12 |
| Panama | 352 | 42 | 32 | 13 | 5 | 8 |

[1] Reference No. 1

**Table 2. Prevalence of hypovitaminosis A in children younger than 15 years.[1, 2]**

| Country | 0-4 years | | 5-9 years | | 10-14 years | | 0-14 years | |
|---|---|---|---|---|---|---|---|---|
| | Percent Prevalence | Number of cases | Percent Prevalence | Number of cases | Percent Prevalence | Number of cases | Percent Prevalence | Number of cases |
| Guatemala | 26.2 | 219,100 | 16.2 | 108,300 | 11.1 | 62,200 | 18.8 | 390,100 |
| El Salvador | 43.5 | 241,200 | 43.5 | 190,700 | 22.4 | 82,300 | 37.8 | 514,200 |
| Honduras | 39.5 | 137,000 | 29.0 | 81,200 | 21.9 | 51,609 | 31.3 | 269,800 |
| Nicaragua | 19.8 | 56,900 | 18.5 | 50,500 | 6.4 | 14,400 | 15.5 | 121,800 |
| Costa Rica | 32.5 | 96,600 | 25.6 | 60,300 | 11.7 | 22,400 | 24.6 | 179,300 |
| Panama | 18.4 | 38,300 | 12.1 | 20,600 | 9.7 | 13,600 | 14.0 | 72,500 |
| TOTAL | 31.2 | 769,100 | 24.7 | 511,600 | 14.3 | 247,000 | 24.4 | 1,547,700 |

[1] Reference No. 1

[2] Based on population estimates of July 1965 and on serum values lower than 20 µg/100 ml

considered of high priority the investigation of means to raise the vitamin A intake, in such a manner that essentially all the population could reach an adequate vitamin A nutritional status.

## DEVELOPMENT OF THE PROCESS OF FORTIFICATION OF SUGAR WITH VITAMIN A

Research was carried out by INCAP, and a process was developed for the fortification of sugar with retinol palmitate as an effective way to prevent hypovitaminosis A. A research and development program was started in 1969 to attempt fortification of a suitable vehicle with vitamin A. The initial immediate objectives were those outlined below.

### Selection of the Dietary Vehicle

A vehicle suitable for this purpose should combine the following characteristics: a) it must be consumed by essentially all the population, b) there must be little variation in its day to day per capita consumption; c) fortification should result in unappreciable change of the organoleptic characteristics and acceptability of the vehicle; and, d) the cost and nature of the vehicle must be such as to allow for an economically feasible supplementation through an industrial process.

On the basis of these characteristics, white sugar[1] was selected as the food vehicle for this project. Initially, table salt was considered. However, subsequent calculations revealed that it did not fulfill requirement (d) due to the low daily per capita salt consumption of the population and its cost. In contrast, sugar fulfilled all characteristics. Besides, sugar production is centralized in a few technically well-equipped and-administered factories, so that the addition of vitamin A would not raise any serious problems.

### Selection of the Vitamin A Preparation

The basic characteristics of the product were established as follows: a) it must be water-miscible or water dispersable; b) it must be appropriate for preparation in the form of a physically stable sugar-based premix, that is, no segregation of the ingredients should occur, c) it must be undetectable by taste, smell, or any other organoleptic characteristic, when mixed with the sugar in the proposed concentrations; d) it must be sufficiently stable when present in a high enough concentration to assure ingestion of vitamin A at a level that would significantly contribute to prevent a deficiency of this nutritional factor in the general population; and e) its cost should not affect significantly the price of the final product.

### Development and Testing of the Process

Tests in the laboratory and at industrial scale were started in 1969. A water-dispersable vitamin preparation especially manufactured for addition to food-stuff intended for human consumption was initially selected.[2] A premix was made with 1 part retinol palmitate and 9 parts sugar. This premix was then added to the sugar in the final stage of the production line by means of a motorized mechanical feeder. In many respects, the process was satisfactory. There was, however, one unsolved problem: the tendency of the retinol palmitate in the premix to separate from the sugar.

In order to solve this problem, an investigation was carried out to obtain a

[1] Centrifuged washed (plantation white) or refined sugar.

[2] Retinol palmitate 250 SD (spray dry) Hoffman LaRoche, Basel, Switzerland, was initially used, later it was replaced by retinol palmitate 250 CWS (cold water soluble) which was found more appropriate.

physically stable (non-segregation) premix. This was achieved by mixing 250 CWS water dispersable retinol palmitate with sugar and a small amount of peanut oil by a process yielding a premix containing 15,000 μg (50,000 IU) g of sugar (see Appendix 1).

The premix thus obtained is also chemically stable. When stored at room temperature (18-32°C) for nine months, without taking any special precautions and exposed to air, there was only a 9 per cent decline in potency. This particular premix was used to test, both in the laboratory and at industrial scale, a new low-cost and very simple process for adding the vitamin to the sugar. This process provides for the addition of the premix in the centrifuge of the sugar manufacturing plant. The main advantages of the process are: a) the system regulates the amount of premix added to the sugar; and, b) it requires neither special equipment for the addition of the premix nor additional personnel. Industrial scale trials made with the new method, which proved very successful, demonstrated its feasibility.

The fortified sugar prepared in this manner at industrial scale was submitted to tests of acceptability, physical and chemical stability, and biological effectiveness in laboratory animal and human subjects, with very satisfactory results (5-7).

By 1971 the research resulted in a process that satisfied all requirements for industrial application and, at the same time, yielded an entirely acceptable fortified sugar.

## National Programs in Central America and Panama

This new approach to combat vitamin A deficiency at population level was strongly promoted among government and nonofficial health-related agencies in Central America.

As a result four countries (Costa Rica, Guatemala, Panama, and Honduras) have passed laws to the effect that all sugar for home consumption be fortified with vitamin A (8) (see Appendix 2, for example).

# Evaluation

Although vitamin A fortification of sugar had proved to be effective in laboratory animals and in small population groups, it was considered that its nutritional effectiveness needed to be assessed in larger population groups. A project for this purpose was, therefore, designed and built into the program at national scale in Guatemala. The basic purpose of the study was the evaluation of the effectiveness of a program of fortification of sugar with vitamin A. It is important to emphasize that *the main objective* of the program was to increase the adequacy of intake of vitamin A and, through this improved intake, to raise the body fluids and blood serum levels among the population at large, increasing thereby the supply of retinol to the tissues.

## BASES AND GENERAL PLAN

### Bases

The evaluation study was based on the premise that the application of a public health intervention program without adequate built-in evaluation was 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; in effect this measure, proposed to solve the problem of hypovitaminosis A, had 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 was successful, that is, if the program was proved effective, many countries would be interested in considering its implementation.

The specific objectives of this project were to evaluate: a) the delivery system of the fortified sugar; b) the nutritional effectiveness, and, c) the cost of the intervention.

### General Plan

The evaluation of the program began in Guatemala immediately before the initiation of the fortification at the national level. The first phase consisted of a nutritional survey with the specific objective of obtaining prefortification 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 obtained.

This baseline study was started in October and concluded in November 1975. In Guatemala effective fortification began in December 1975. According to the evaluation plan, four additional nutritional surveys followed the initial one at intervals of six months during the years 1976 and 1977. The central purpose of this experimental design was to determine the changes in the parameters being measured, which would reveal the extent of the biological effectiveness of the fortification program.

The first follow-up survey was carried out during April-May 1976 (dry season), the

second during October November 1976 (rainy season), the third during April May 1977, and the last during October November 1977. In Figure 1 a diagram illustrating the project schedule is shown. The dietary, biochemical, and clinical surveys were thus repeated every six months for the two year period. This was justified by the need to collect data coinciding with the two main seasons (dry and rainy), which may have affected the availability of food sources of vitamin A, mainly from vegetable origin (carotenes).

The surveys were planned to be carried out in 12 rural communities of Guatemala with populations between 1,000-2,000 inhabitants. These communities were selected at random by statistical methods and are representative of the principal rural ecologic areas of the country. Within each community 30 families were randomly selected. Details of the statistical bases, methods, and procedures of the sampling process are described elsewhere in this report (see "Sampling").

The major variables investigated in relation to the efficiency of the delivery system were the actual consumption of fortified sugar by the families in the study and the estimated intake of retinol from that "new" source of vitamin A, throughout the two years of fortification.

For the purpose of evaluating the nutritional effectiveness of the program, the investigation of the following variables was given primary importance: a) blood serum retinol levels of children under 6 years of age; b) retinol content of breast milk from rural women who were breast feeding at the time of the surveys; c) clinical and anthropometric examination of children under 6 years of age with particular emphasis on eye lesions attributable to vitamin A deficiency. Ancillary data were obtained about general morbidity present in the same children at the time of the clinical examination. A complementary study was also carried out in relation to the effect of the fortification on liver reserves, determining liver retinol concentrations in individuals of all ages who died from accidental causes in Guatemala City throughout the two year study period.

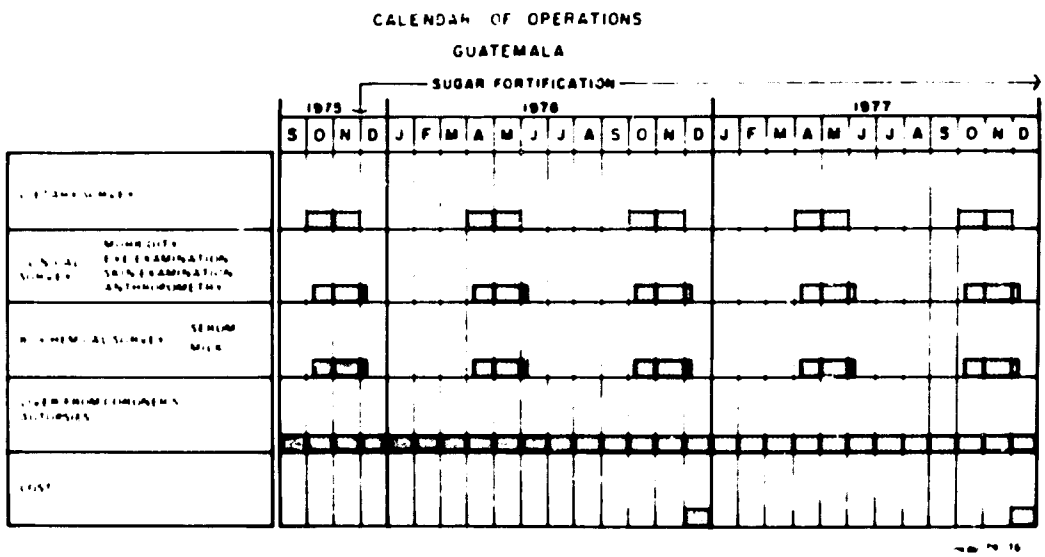


**Figure 1. Diagram of the project schedule.**

## METHODS AND RATIONALE OF THE PARAMETERS SELECTED AS INDICATORS OF CHANGE

### Delivery System

The ultimate purpose of the methods and procedures used to study the delivery system was to determine: the total amount of sugar that was fortified; the efficiency with which the process was carried out at the sugar factories including the level of fortification (that is, the estimated micrograms of retinol per gram of sugar), and the extent to which the fortified sugar reached the consumers.

A specific guide to carry out the operations involved in the supervision and control of the fortification has been published in the form of a manual (*9*).

The delivery system was assessed at two levels:

*National and factory level.* Information was obtained on the total production of white sugar for local consumption. In addition, the total production of white sugar and the actual amount of the vitamin A premix applied at the production line of each sugar factory were verified. Special forms where this information was recorded weekly were submitted to the central level in order to keep control of the process and introduce adjustments when considered necessary. From those data, an average (estimated level) of fortification was derived. Optimal efficiency was considered when the ratio of 1 sack of 25 kg of premix per 544 qq sacks (1 qq sack = 46 kg) of sugar was obtained. This ratio corresponded to a dilution of 1:1 000 of the 15 000 µg retinol/g premix, at the factory, yielding a final fortified sugar containing 15 µg (50 IU) per gram of sugar. Chemical analysis was carried out occasionally on samples collected from the factories and from some large market outlets.

*Consumers level.* In order to determine if the fortified sugar was reaching the target population, samples of sugar were obtained from the households and the retail shops of each of the 12 rural villages under study and tested for retinol content using the rapid colorimetric procedure described in Appendix 3. This sample collection was systematically done by the dietary team during each survey. In addition, a group of less accessible and smaller villages (< 500 inhabitants) was also visited (August–September 1977) to obtain sugar samples in the same manner as described for the 12 villages of the main study sample. These villages were chosen among those that were related by geographic location to the 12 communities of the original study sample but significantly removed from them.

Two further studies conducted independently in five villages (69 to 220 inhabitants) were carried out in this lower socioeconomic population stratum in order to determine whether white sugar was being consumed by the families and the level of intake (*10, 11*).

Through this approach, the per cent of sugar samples which were fortified was found. An integration of all the data obtained from the factories and from the villages allowed a rough over the time and overall estimate of the mean contribution of sugar consumption to the intake of vitamin A by the people, that is, how many micrograms of retinol they took per gram of sugar consumed. For the dietary computation of intake of retinol equivalents a "new" item (fortified sugar) was added to the food composition table. As will be seen under "Results," its computed retinol contribution came out to be around 10 µg/g of sugar.

In summary, with the information collected from the communities and the factories, estimates could be made of the retinol actually reaching the target population through fortified sugar.

### Sampling

*Bases.* The following epidemiologic characteristics of the hypovitaminosis A problem in Guatemala were considered basic to determine the type of population sample for the study: a) the dietary deficit of vitamin A food sources affects generally and most severely the rural low socioeconomic group; b) it is recognized that among this large sector of population, the most vulnerable

groups are the preschool child and, because of her markedly increased physiologic needs, the lactating woman.

Therefore, the construction of sampling frames was restricted to a target population defined as an aggregate of rural communities, vulnerable to vitamin A deficiency. Two general criteria were considered: size of the communities, and accessibility to the communities. The sampling proceeded in two stages. In the first stage a sample of 12 communities was drawn; the communities selected and their geographic distribution are shown in Figure 2. In the second stage a sample of occupied dwellings (representing "families") was selected from the chosen communities. The family sampling was carried out using updated maps of each selected community, in which all occupied dwellings had been properly identified. This was accomplished by visits to the communities by technicians with previous experience in this type of work. The selection of families (dwellings) for each survey was carried out using systematic sampling with random start.

*Procedures and actual sample selected.* In the following paragraphs, general procedures for selecting communities are described. Results of the nutritional survey of Central America and Panama (*1*) showed that small rural communities could serve as effective indicators of the fortification program since high prevalence of low serum

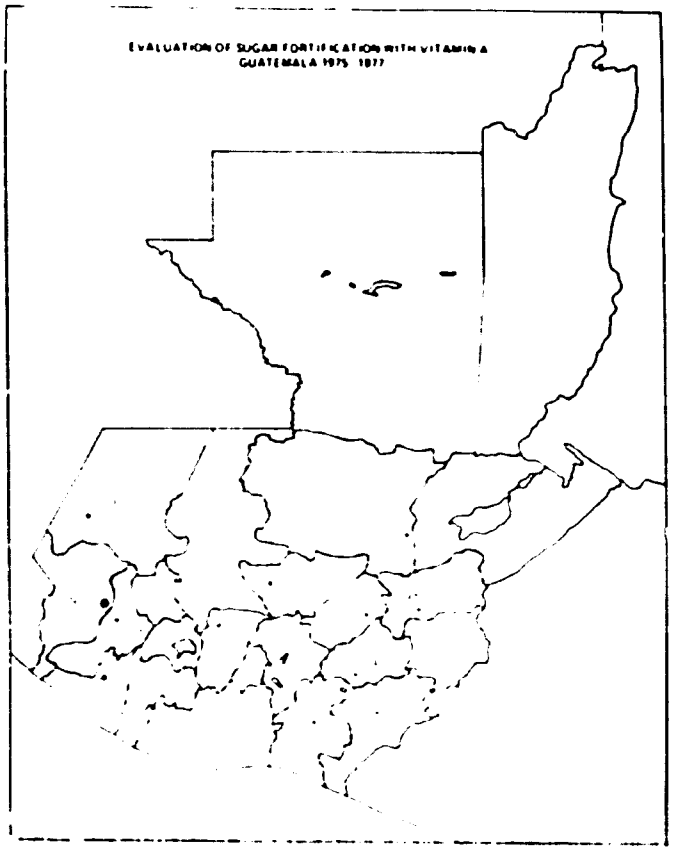


**Figure 2. Communities selected and their geographic distribution.**

vitamin A levels had been well documented in these populations.

A stratified random sampling procedure, taking into account geographic distribution, was followed. The process was restricted and used in communities or villages reported to have 1,000 to 2,000 inhabitants, since there was sufficient information to construct appropriate sampling frames for this type of communities. On the other hand, it was thought that communities with less than 1,000 inhabitants represented widely dispersed populations of difficult access, without the required information for constructing appropriate sampling frames. However, the available epidemiologic information suggested that the general conditions of these smaller populations were quite similar to those of the somewhat larger communities (1,000–2,000 inhabitants) used in the construction of the sampling frame of this project.

In general, the delivery systems for merchandise, including the fortified sugar, are more effective for communities with significantly more than 2,000 inhabitants. These larger communities have better access to markets and easier contact with urban centers. For this reason, changes induced by the consumption of the fortified sugar in the smaller communities of fairly difficult access used as indicators for this project are logically expected to occur also in the larger communities that have more favorable conditions for the delivery of the fortified sugar. In other words, the biological demonstration of beneficial effects in this sector of the population could be interpreted as evidence of similar or greater benefits in communities with better communications, provided an effective delivery of the fortified sugar could be demonstrated in these communities. Accordingly, and in consideration of cost, the larger populations (> 2,000 inhabitants) were not included in the sampling.

In general, in Guatemala, communities with 1,000 to 2,000 inhabitants have fairly difficult access; roads are few and all too often the only means of access to these communities is by dirt roads or footpaths. Also, socioeconomic and sanitary conditions are uniformly poor and characteristic of those described for rural communities of low socioeconomic level in Latin America.

In summary, the construction of a sampling frame restricted to communities with 1,000 to 2,000 inhabitants was considered to ensure that the detailed studies conducted by this project would be concentrated in the population from whom a problem of vitamin A nutrition had been documented, having unfavorable sanitary and socioeconomic conditions and being not easily reached.

Using the sampling frame constructed for these communities, a proper sampling system was devised to ensure that the estimates obtained for the sample were applicable to rural communities of similar characteristics at the national level. The sample size was estimated adequate to ensure the reliability of the data and sufficient sensitivity to detect changes as these occurred. The critical estimator selected among those included in the study for defining the sample size was the proportion of preschool children with low levels of serum retinol. 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 survey of Central America and Panama (*7*) showed that, in Guatemala, the prevalence of low serum retinol values (less than 20 $\mu$g/100 ml) in children of preschool age oscillated around 25 per cent, and on this basis a sample of 300 children of preschool age was estimated to permit the identification of a net change of 10 per cent units in the baseline prevalence of low serum levels. In other words, a sample of

this size was deemed sufficiently large to permit the measurement of a reduction in the population from the 25 per cent baseline prevalence of low serum retinol values to a prevalence of 15 per cent. This level of sensitivity was considered appropriate for the objectives of the present evaluation program.

According to what has been described and based on data from the National Census of Guatemala for 1973, 12 rural communities between 1,000 and 2,000 inhabitants were randomly selected.[3] A census carried out directly by investigators of the present research project during 1975-1977 (see Appendix 5), allowed for confirmation or correction of the figures obtained from the 1973 census (Table 3). It was revealed then that four communities out of the 12 selected before had less than 1,000 inhabitants, these were: San Rafael, Saquitacaj, La Libertad, and Cahaboncito (with 760, 771, 935, and 876 inhabitants, respectively). The difference is attributed to the fact that the information from the 1973 national census included all the people living in a larger geographic area around the community, which belong to its political limits. On the other hand, the census carried out directly by the investigators included only the people in the actual "urban" limits of each community.

The 12 villages represent the main ecologic zones of the country: the west highland plateau (La Libertad, San Rafael, Buena Vista, and Saquitacaj); a small agriculture parcel in the south lowlands (Santa Fé); the dry northeast region (San Juan and El Jicaro); the mountainous region of the east (San Carlos, Ixhuatán, and El Barreal); the region of the central plateau (Cubulco); and the north region (Cahaboncito).

Of these, four communities are predominantly Indian: Buena Vista and San Rafael ("Mam" group), Saquitacaj ("Cakchiquel" group) and Cahaboncito ("Quekchi" group). Cubulco has a mixed population of *ladino*[4] and Indian of the "Quiché" group. Some of the ecologic and socioeconomic characteristics of the 12 communities are given in Appendix 4.

## Dietary Studies

To estimate the vitamin A intake of the population from the different communities, the food consumption of the families was studied using the 24-hour recall method as described by Flores et al. (*12*). To obtain this information the homes were visited to interview the mothers (or heads of households) and determine food portion sizes by direct weighing. Particular attention was paid to the intake of white sugar and food sources of retinol and carotenes including manufactured products (fortified foods, vitamin pills, etc.). Scales in grams (Hanson brand), with a capacity of 500 g, were used to weigh the foods.

Previous to the field work, two weeks were spent in special training of the field personnel in charge of the dietary study. The persons selected were graduate teachers (high school level) with some knowledge of food habits of the country. Special forms were prepared to obtain the family food intake. Samples of these forms are enclosed in Appendix 5. Interpretation of the food data in terms of nutrients was based on the INCAP-ICNND Food Composition Table, corrected for vitamin A according to Flores et al. (*13*). A special form was used to obtain

[3] The Department of El Petén was excluded because the number of villages between 1,000 and 2,000 inhabitants was very small; that department had the least density of population, and communication facilities were extremely difficult. Its large territory held only 1.2 per cent of the total population. (Bureau of Statistics, Guatemala, 1976)

[4] *Ladino*, unlike Indians, descendants and heirs of the Mayan culture; *ladinos* speak Spanish; the two groups are linguistically and culturally different.

Table 3. Census data from the 12 rural communities.[1]

| Community | No. of families | Population | Children | | Pregnant women No. | Lactating women No. |
|---|---|---|---|---|---|---|
| | | | 0-11 months | 12-71 months | | |
| El Barreal | 210 | 1123 | 50 | 207 | 19 | 4[illegible] |
| Santa María | 331 | 1651 | 68 | 233 | 26 | 51 |
| San Juan | 225 | 1233 | 60 | 19[illegible] | 14 | 51 |
| El Jícaro | 384 | 1931 | 73 | 314 | 21 | 58 |
| Buena Vista | 161 | 1139 | 42 | 188 | 8 | 35 |
| San Rafael | 137 | 760 | 39 | 144 | 7 | 35 |
| Saquitacaj | 1[illegible]0 | 771 | 36 | 12[illegible] | 6 | 36 |
| La Libertad | 169 | 935 | 37 | 187 | 12 | 37 |
| Cubulco | 307 | 1536 | 56 | 223 | 17 | 57 |
| San Carlos | 288 | 1327 | 72 | 236 | 17 | 71 |
| Cahaboncito | 163 | 876 | 46 | 160 | 12 | 44 |
| Santa Fe | 221 | 1292 | 64 | 244 | 1[illegible] | 54 |
| TOTAL | 2,736 | 14,574 | 653 | 2,464 | 185 | 572 |

[1] These population data were obtained during the present surveys and were used to correct the data from the national census

data on sugar, not only the amounts but also the origin, in order to identify the shops or markets where the sugar had been obtained by the families and, if possible, the manufacturer.

The field operation was carried out as follows: each Monday for six weeks, four field workers travelled to the communities. On Tuesday, Wednesday, and Thursday they collected the dietary information of the families randomly selected; each worker investigated five families each day. On Friday they returned to the office to revise the dietary records obtained. Two persons were in charge of the checking of the filled out forms and of the preliminary dietary tabulations.

The 360 families distributed among the 12 communities were studied in six weeks, since two communities were covered simultaneously per week. Every week, 60 family forms were received in the office for revision and correction. After the collection of the dietary data, two additional weeks were spent to finish the revision of the forms by the same field workers. The "clean food data" were then ready to be processed at the computer center of INCAP.

In each community visited by the dietary team, samples of white sugar were collected from the homes in the sample and from the retail shops of the community to determine, by laboratory procedures, if they were fortified. In addition, the dietary workers collected the breast milk specimens for the biochemical study, as will be described in another section.

Besides the main family dietary survey just described, dietary surveys were performed directly on the preschool child (this, however, was done only in two of the five consecutive surveys carried out). In addition, a sugar consumption survey was carried out in 12 rural villages of less than 500 inhabitants in order to determine whether the delivery system reached communities smaller than those of the main study sample.

The information obtained regarding the intake of vitamin A from natural foods was used to determine the adequacy of the dietary intake of this nutrient from natural sources. Adequacy was calculated by comparison with the recommended intakes of retinol equivalents proposed by INCAP (2). Data on sugar intake and on the estimated retinol content of fortified sugar were used to calculate the additional vitamin A which the families were obtaining from this source and the extent to which adequacy of intake was improved by the consumption of fortified sugar. The data collected through the five consecutive surveys carried out six months apart during two years were also necessary to confirm the degree of stability of the level of vitamin A intake from natural food sources through the study period. This information was considered basic to determine whether the changes detected in the biological indicators could be attributed with confidence to the vitamin A consumed with the sugar, rather than to variations in the intake of vitamin A from natural dietary sources.

**Biochemical Studies**

The principal aim of these studies was to obtain data on the serum retinol levels of 1-5 year old children and on the retinol content of breast milk from the lactating women present in the families. The biochemical field team visited each community on a scheduled day, accompanying the clinical team. The families were requested to attend a "center" (health post, school building, or similar facility) in the morning of that day. Blood samples were taken by laboratory field workers who were expert technicians experienced in venipuncture as well as specially trained in the handling, preservation, and transport of the specimens.

Five milliliters of venous blood were obtained from the antecubital vein using new vacutainer tubes, without anticoagulant, and disposable needles. The specimens were carefully labelled with the standard identification code, refrigerated in an icebox, and properly packed for their transport to INCAP laboratories. In all cases they reached the laboratory on the same day. Upon arrival the serum was separated from the clot by refrigerated centrifugation at 1,600 × g, and frozen at −20°C until analyzed. Hemolysis and exposure to light were avoided at all times.

The breast milk samples were obtained by the dietary team, which visited each community on the week preceding the visit of the biochemical team. The procedure for taking these milk specimens had been proved feasible, easy, and well accepted by the mothers during previous INCAP studies (7). The lactating mothers were instructed to extract themselves around 8 ml of milk, when possible from a full breast, into a clean 10 ml test tube specially provided. The emphasis on obtaining the specimen from a "full breast" was to facilitate the extraction but also to standardize the procedure, since it is known that the concentration of some milk components tends to increase as the breast content gets to the last residual portion. The specimens were immediately placed in ice and preserved refrigerated at 4° to 8°C until reaching INCAP laboratories. Under any circumstances, the milk specimens were frozen at −20°C within 24 hours of collection. Exposure to direct light was avoided.

Retinol was determined in both serum and milk specimens by the absorbency of a xylene-kerosene extract of the saponified aliquots at 328 nm before and after complete destruction of the retinol by strong ultraviolet irradiation. The method is essentially that described by Bessey et al. (14).

In view of the fact that the retinol concentration in biological materials (blood serum, breast milk, and liver) was most fundamental for evaluating the nutritional effectiveness of the fortification program, a strict laboratory control was kept throughout the two year study period regarding its reproducibility. Under laboratory conditions, each sample was always run in duplicate. The reproducibility was checked on repeated occasions with replicates of the same sample analyzed in one laboratory run. The coefficient of variation under these conditions was always less than 2 per cent.

In addition, since the study lasted about two years, it was very important to check the consistency of the method as run day by day. For this purpose, control sera were aliquoted in many replicates, which were then frozen at −20°C. With every batch of experimental samples, two aliquots of the control serum were also analyzed. In this manner, the variability of the method from day to day throughout the study period could be determined. Table 4 gives a summary of the data obtained, showing the magnitude and consistency of the variability. One could then be sure that the results obtained at any point in time during the study period were comparable to any other. This control system allowed also to detect immediately if anything was going wrong with the method, in order to make the necessary adjustments and corrections. It has also been shown in the laboratory that storage of samples at −20°C for over two years does not alter the retinol value as determined by the method used.

The bases for the biochemical indicators selected were as follows. The nutritional nature and objectives of the fortification of sugar with vitamin A have already been mentioned. In this nutritional context, the high prevalence of decreased levels of retinol in blood serum of preschool children and in breast milk was considered basic to the approach for designing the evaluation

program. Accordingly, the principal indicators chosen to detect and measure the impact of the fortification were blood serum levels of preschool children and levels of retinol in mothers' milk.

The rationale for the decision to study blood of only preschool children was 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 was shown for this age group, the unavoidable conclusion had to be that older children and adults are also benefitted, and perhaps even more.

The concentration of retinol in blood serum has proved very useful to assess 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 (*15*) and by the International Vitamin A Consultative Group (IVACG) (*16*). Data from the Sheffield experiment (*17*), confirmed by epide

**Table 4. Quality control of the method for the determination of retinol throughout the study period.**

| Dates | Control Serum | No. individual determinations(1) | $\bar{x}$ | S.D. |
|---|---|---|---|---|
| Oct 09 - Oct 30, 75 | 1 | 4(2) | 36.17 | 1.40 |
| Nov 07 - Nov 17, 75 | 1 | 6 | 36.56 | 1.12 |
| Mar 01 - Apr 13, 76 | 2 | 18 | 33.55 | 1.31 |
| Apr 21 - May 12, 76 | 3 | 10 | 67.64 | 1.55 |
| May 12 - Jun 04, 76 | 4 | 14 | 26.02 | 0.65 |
| Jun 04 - Jul 15, 76 | 5 | 14 | 20.23 | 1.20 |
| Jul 20 - Jul 23, 76 | 6 | 5 | 13.59 | 0.77 |
| Jul 27 - Aug 26, 76 | 7 | 16 | 37.98 | 0.80 |
| Jan 20 - Feb 10, 77 | 8 | 8 | 43.95 | 1.52 |
| Feb 10 - Mar 30, 77 | 9 | 15 | 52.51 | 1.06 |
| Mar 30 - May 05, 77 | 10 | 12 | 59.87 | 1.90 |
| May 13 - Jun 23, 77 | 11 | 17 | 70.75 | 0.68 |
| Oct 06 - Nov 06, 77 | 12 | 17 | 68.45 | 1.30 |
| Nov 06, 77 - Jan 10, 78 | 13 | 7 | 37.70 | 2.07 |
| Jan 10 - Feb 27, 78 | 14 | 11 | 35.97 | 1.11 |

(1) Individual determinations run independently in duplicate on different days

(2) Beckman DU; all other Variant Model 635

miologic observations and interpreted by the Group of Experts of the ICNND (*3*), served to elaborate the guide for the interpretation of blood retinol levels shown below:

**Plasma retinol (µg/100 ml)**

| Deficiency | Low | Acceptable | High |
|---|---|---|---|
| 10 | 10-19 | 20-49 | ≥ 50 |

More recently Sauberlich et al. (*4*) have concluded experiments in humans whose results encouraged them to suggest the level of 50 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 50 µg/100 ml would be necessary to ensure modest body stores of the vitamin. Therefore, the data obtained on the preschool children in the rural sample have been analyzed in terms of their distribution by category groupings of < 10, 10-19, 20-29, and 30 or more µg/100 ml. One criterion to judge the effectiveness of the program was the proportion of children who moved from the "deficient" and "low" to the "acceptable" category. A statistically sounder criterion was the modification of the shape and the shift to the right of the distribution curve of serum values, as suggested by IVACG (*16*).

The rationale for the study of the vitamin A content of breast milk was based on previous studies in Central America showing very low average values in lactating women from rural areas of Guatemala (*6*) and El Salvador (*7*). In effect, since retinol is not synthesized by the mammary gland, but is instead taken up from the mothers' retinol pool, their poor vitamin A intakes are reflected by marked decreases of retinol content in their breast milk. It had also been demonstrated that if the families replace palm by fortified sugar and the women consume fortified sugar during the last trimester of pregnancy and the first four months of lactation, there is a positive effect on the vitamin A content of their breast milk and on the serum levels of the mothers and their infants (*7*).

Furthermore, the study of human milk was considered essential because of the fact that in the type of population under study, infants are breast-fed with insignificant supplementary foods for an average of 1-1/2 years and, therefore, it was important to know the extent to which the program would improve the vitamin A intake of the breast-fed babies. Values of vitamin A content of breast milk from well-nourished lactating women are expected to be around 19 µg/100 ml (*18*). The data obtained in the present study were judged in relation to this acceptable value and fractions of it, such as 20 and 30 µg of retinol per 100 ml of milk, as well as in terms of the shifts in the population distribution curve of milk retinol values.

## Ophthalmologic and Clinical Observations

All children under 6 years of age were examined for signs of xerophthalmia by the physician who had been specially trained for this purpose by an expert ophthalmologist before the beginning of the first survey.

Signs were recorded on a special form (see Appendix 5). They were then classified according to the degree of xerophthalmia encountered. The signs were recorded in such manner as to allow their classification as proposed by WHO (*19*).

Corneal ulcerations and keratomalacia are the last events in the chain of clinical manifestations of vitamin A deficiency. Cases of these conditions occur most commonly in children who are severely protein-calorie malnourished and have also a low vitamin A nutrition, the severe corneal lesion being often 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 xerophthalmia among samples of ambulatory population generally do not give a true picture of the damage caused by vitamin A deficiency, including that of the eye. It would be wrong to conclude that there is no serious vitamin A deficiency problem from results obtained through this clinical approach only. 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 the countries of Central America. They are, however, abundant in pediatric wards of public hospitals. 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: the proportional part that can be seen "over the water surface" (kwashiorkor or xerophthalmia) is insignificantly small compared to the "hidden, underwater" portion of the problem (chronic, subclinical deficiency; biochemical and physiological damage; population at risk of developing severe clinical damage and appearing over the surface).

Despite these considerations, it was deemed important to conduct a careful ocular examination in all children studied, for the following reasons: a) if cases with active xerophthalmia lesions were found, immediate medical care would be indicated, and, b) to document the existence of such cases of ocular damage that represent the visible peak of the iceberg, and to analyze the individual characteristics or environmental factors that may have caused or contributed to the development of the severe eye lesions.

General morbidity data were obtained for each child by direct clinical examination and history by a clinician and were recorded in a special form (see Appendix 5).

The results of the general morbidity examination were deemed important to determine the interrelation between vitamin A status and "morbidity load" of the children. In fact, the synergistic interrelation between vitamin A deficiency and infections has been well recognized (*20, 21*). Recently, Arroyave and Calcaño (*22*) have confirmed the marked depressing effect of infections on retinol serum levels of both children and adults.

Body weight was taken with a platform scale (Continental Scale Corp., Illinois, USA) for the children over 12 kg and with an infant clinical scale (Seca, West Germany) for those under 12 kg; these scales were routinely checked using a standard weight. Body length was measured in centimeters with an infantometer, in the supine position for children under 2 years, and in the upright position for older children, using the standardized procedures. Height and weight were taken from all children, and their general level of nutrition assessed on the basis of weight for age, height for age, and weight for height (*23*). The biochemical results were expressed by level of nutrition, before and after fortification.

## Additional Biological Studies

Besides the parameters described, which were measured at the five consecutive surveys conducted at six-month intervals during the two-year period on samples of the 12 communities, the retinol content was determined in liver specimens collected from coroner autopsies in Guatemala City in a continuous manner, starting before the time fortification became effective. By agreement with the chief coroner in the city and his deputies, liver samples from autopsies performed in accidental deaths were collected and analyzed for retinol. Each sample was accompanied by informa

tion registered on a special form (see Appendix 5) on the age, sex, occupation, cause of death as determined after the autopsy, place of death, and date and hour of autopsy. The liver specimens, consisting of a fragment of approximately 20 g taken systematically from the right lobe, were obtained as soon as possible after death and preserved frozen at −20°C until analyzed. Vitamin A was determined in a distilled water homogenate by an adaptation of the method of Bessey et al. (*14*).

Although the amount of vitamin A present in the liver of Central Americans had not been measured, it was reasonable to assume, on the basis of consumption and serum data, that a cross-sectional study would show a wide range with a significant proportion of low concentrations and maybe a few individuals with high levels. A basic assumption was that throughout the study period, a general trend upwards would be observed, with a decrease in the number of cases with low concentrations. No significant change was expected to occur in the high levels since the amount of vitamin A provided with the sugar was not considered sufficient to generate any important overaccumulation in the liver. This study was, as mentioned before, only carried out in Guatemala City, and therefore it is not representative of the overall population. Nevertheless, since all samples available meeting the basic criteria were taken without any bias, the changes observed with the fortification must be the reflection of the effect of the intervention in this large urban center.

### Cost of Fortification and Control

A study of cost was conducted at the end of the first and of the second year of fortification, with data from the National Association of Sugar Manufacturers of Guatemala on the vitamin A, the manufacturing of premix, and the operation of fortification itself. At the same time an assessment was made of the cost of the control process, including a routine collection of sugar samples, analysis, and monitoring of the process in the mills. Cost data were expressed as: a) total cost per year to the country; b) cost per pound of sugar fortified; c) cost per inhabitant per year; and, d) cost per person "protected" per year.

To estimate the extent of the population "protected" by the intervention, a comparison was made between prevalence of "deficient" and "low" serum vitamin A levels before and after. Calculations were made accepting as cut-off points the levels of 10 and 20 $\mu$g of vitamin A per 100 ml of serum.

### Statistical Analysis

The data obtained from the various studies were processed in a computer H.P. 3000 and submitted to statistical testing by standard methods (*24*).

## RESULTS

Within the period of two years of evaluation, the sugar was fortified at the national level during the two sugar production seasons (*zafras*), from December 1975 through June 1976 and from December 1976 through June 1977. During each of these production seasons all the year-demand of white sugar for local consumption is produced. The results to be presented in this section are the "expression of change" corresponding to the implementation of this nutritional intervention. Modifications of the pre-fortification vitamin A intake and nutritional status of the population revealed by these results are to be related to the additional amounts of retinol that became available to the Guatemalan population.

## Delivery System

Tables 5 and 6 present the data obtained through the system of supervision and control described under "Methods." According to these data, 75 and 72 per cent of the reported total white sugar produced were fortified. The "fortification ratio" (see Tables 5 and 6) comes out to be 628 for 1976 and 574 for 1977, instead of the mean theoretical ratio of 544 qq of sugar for every 25 kg sack of premix used. This ratio of 544 would give a sugar containing 1 part of premix per 1,000 parts of sugar, that is, 15 μg (50 IU) of retinol per gram. On this basis, the sugar fortified during the 1975-1976 season would contain 13 μg/g and that from the 1976-1977 season would have 14 μg/g. Combining these sets of data, and assuming that each family consumed sugar with and without vitamin A distributed at random through the two years, one can compute the equivalent contribution of the food item *fortified sugar* as containing 9.8 and 10.1 μg retinol per gram for 1976 and 1977, respectively, as a "throughout mean" (13 × 75/100 and 14 × 72/100, respectively).

As explained under "Methods," samples of white sugar were collected from households and retail stores by the field teams and were tested for retinol content by the semi-quantitative procedure described in Appendix 3. Tables 7 and 8 give an account of the results. It can be seen in Table 7 that in the 12 rural communities selected as the study sample, the proportion of fortified sugar specimens varied from 61 to 81 per cent in household specimens and from 62 to 75 per cent in retail stores for the survey periods carried out after the initiation of the fortification program. The samples obtained during August-September 1977 from the 12 additional smaller communities (less than 500 inhabitants) gave essentially the same average results, as shown in Table 8. These data collected at the village level agree with the proportion of the total sugar production which was fortified in accordance with the information from the sugar factories (Tables 5 and 6). This strengthened the decision to use the figure of 10 μg/g for the estimation of the dietary contribution of sugar to the vitamin A intake of the population of Guatemala once the fortification program was underway.

When the level of fortification was calculated by the "fortification ratio" described above and compared with the chemical analysis of the corresponding sugar samples obtained from the factories, a comparable result was obtained as shown by the average of 12.0 ± S.D. 4.7 and 12.4 ± S.D. 5.2, respectively (n = 13). This led to the decision to use the "fortification ratio" method to estimate the level of fortification at large. The latter approach had the additional advantages of being easy to implement, not involving costs, and being applied in a continuous manner throughout the process in each factory. The chemical data, however, were also useful to reassure the personnel in charge of the possible double control of their efficiency, and as a way to warn the sugar factories about deviations and irregularities in the process of addition of the premix, in order to recheck and correct their system.

## Sample Success

The bases, methods, and procedures used in selecting the sample for the dietary, biochemical, and clinic-anthropometric studies, as described in a previous section, were strictly followed under the supervision of the project statistician.

For the dietary survey the degree of success to cover the original sample was nearly 100 per cent. In effect, essentially all the families in the 12 communities selected were visited and investigated, as detailed in Table 9. This very high coverage is understandable if one considers that the dietary

Table 5. Supervision and control of the fortification of sugar with vitamin A, Guatemala, 1975 1976.

| "Ingenio" (Sugar factory) | Sugar production (in qq=46 kg sacks) | | | | | Premix (25 kg sacks) | | | Fortification ratio[1] |
|---|---|---|---|---|---|---|---|---|---|
| | Fortified | % | Non-fortified | % | Total | Delivered | Used | Left-over | |
| El Baúl | 57,499 | 38 | 92,900 | 62 | 150,399 | 115 | 115 | 0 | 500 |
| Madre Tierra | 299,886 | 100 | - | 0 | 299,886 | 208 | 208 | 0 | 1,442 |
| San Diego | 193,703 | 96 | 7,583 | 4 | 201,286 | 360 | 360 | 0 | 538 |
| Concepción | 450,022 | 82 | 96,838 | 18 | 546,860 | 599 | 599 | 0 | 751 |
| Pantaleón | 259,335 | 53 | 232,000 | 47 | 491,335 | 472 | 472 | 0 | 549 |
| La Unión-Los Tarros | 450,520 | 65 | 239,433 | 35 | 689,953 | 775 | 775 | 0 | 581 |
| Tulula | 29,892 | 41 | 42,435 | 59 | 72,327 | 55 | 55 | 0 | 543 |
| Palo Gordo | 492,867 | 83 | 98,894 | 17 | 591,761 | 928 | 928 | 0 | 531 |
| El Salto | 430,104 | 84 | 79,454 | 16 | 509,558 | 694 | 694 | 0 | 620 |
| Santa Ana | 440,054 | 78 | 123,674 | 22 | 563,728 | 729 | 729 | 0 | 604 |
| Santa Teresa | 28,000 | 39 | 44,445 | 61 | 72,445 | 50 | 50 | 0 | 560 |
| La Sonrisa | 5,435 | 30 | 12,605 | 70 | 18,040 | 10 | 10 | 0 | 543 |
| Total | 3,137,317 | 75 | 1,070,261 | 25 | 4,207,578 | 4,995 | 4,995 | - | 628 |

[1] Fortification ratio = $\frac{\text{number of 46 kg sacks (qq) of fortified sugar}}{\text{number of 25 kg sacks of premix}}$

**Table 6. Supervision and control of the fortification of sugar with vitamin A, Guatemala, 1976-1977.**

| "Ingenio" (Sugar factory) | Sugar production (in qq=46 kg sacks) | | | | | Premix (25 kg sacks) | | | Fortification ratio[1] |
|---|---|---|---|---|---|---|---|---|---|
| | Fortified | % | Non-fortified | % | Total | Delivered | Used | Left-over | |
| El Baúl | 157,920 | 87 | 22,745 | 13 | 180,665 | 327 | 305 | 22 | 518 |
| Madre Tierra | 327,444 | 93 | 23,985 | 7 | 351,429 | 429 | 429 | 0 | 518 |
| San Diego | 147,424 | 69 | 65,170 | 31 | 212,594 | 286 | 286 | 0 | 515 |
| Concepción | 467,320 | 68 | 217,578 | 32 | 684,898 | 1060 | 1060 | 0 | 441 |
| Pantaleón | 618,449 | 74 | 220,359 | 26 | 838,808 | 870 | 870 | 0 | 711 |
| La Unión | 16,588 | 11 | 138,685 | 89 | 155,273 | 75 | 29 | 46 | 572 |
| Los Tarros | 498,066 | 91 | 46,696 | 9 | 544,762 | 1000 | 884 | 116 | 563 |
| Tulula | 34,500 | 57 | 25,772 | 43 | 60,272 | 60 | 38 | 22 | 908 |
| Palo Gordo | 579,966 | 97 | 18,033 | 3 | 597,999 | 1168 | 1153 | 15 | 503 |
| El Salto | 0 | 0 | 534,523 | 100 | 534,523 | 100 | 0 | 100 | - |
| Santa Ana | 620,000 | 96 | 28,591 | 4 | 648,591 | 1170 | 951 | 219 | 652 |
| Santa Teresa | 59,841 | 75 | 20,342 | 8 | 80,183 | 135 | 135 | 0 | 443 |
| Total | 3,527,518 | 72 | 1,362,479 | 28 | 4,889,997 | 6680 | 6140 | 540 | 574 |

[1] Fortification ratio = $\frac{\text{number of 46 kg sacks (qq) of fortified sugar}}{\text{number of 25 kg sacks of premix}}$

**Table 7. Sugar specimens with vitamin A collected in the 12 rural communities of the study sample.**

| Survey periods | Number and percent of sugar specimens: In households | | | | In retail stores | | | |
|---|---|---|---|---|---|---|---|---|
| | n | Neg. | Pos. | (%Pos.) | n | Neg. | Pos. | (%Pos.) |
| Apr-May 1976 | 220 | 86 | 134 | (61) | 44 | 13 | 31 | (70) |
| Oct-Nov 1976 | 252 | 83 | 169 | (67) | 73 | 28 | 45 | (62) |
| Apr-May 1977 | 247 | 77 | 170 | (69) | 87 | 24 | 63 | (72) |
| Oct-Nov 1977 | 288 | 54 | 234 | (81) | 91 | 23 | 68 | (75) |
| Total | 1007 | 300 | 707 | (70) | 295 | 88 | 207 | (70) |

**Table 8. Sugar specimens with vitamin A collected in the 12 rural communities with less than 500 inhabitants, Guatemala, August-September 1977.**

| Community | Number and percent of sugar specimens: In households | | | | In retail stores | | | |
|---|---|---|---|---|---|---|---|---|
| | n | Neg. | Pos. | (%Pos.) | n | Neg. | Pos. | (%Pos.) |
| Cerro Grande, El Barreal | 29 | 11 | 18 | (62) | 6 | 2 | 4 | (60) |
| La Esperanza, Ixhuatán | 41 | 33 | 8 | (20) | 9 | 8 | 1 | (11) |
| Los Tablones, San Juan | 15 | 3 | 12 | (80) | 4 | 1 | 3 | (75) |
| El Zapote, El Ilícaro | 22 | 13 | 9 | (40) | 5 | 1 | 4 | (80) |
| La Esperanza, Octunculco | 19 | 2 | 17 | (89) | 5 | 0 | 5 | (100) |
| Siquival, San Rafael | 25 | 1 | 24 | (96) | 6 | 1 | 5 | (83) |
| Sta. Esperanza, Saquitacaj | 15 | 2 | 13 | (87) | 4 | 2 | 2 | (50) |
| Trapichillo, La Libertad | 22 | 0 | 22 | (100) | 6 | 0 | 6 | (100) |
| Chicusnitin, Cabricán | 14 | 8 | 6 | (43) | 7 | 1 | 6 | (86) |
| La Crénaga, Alzatate | 27 | 4 | 23 | (85) | 7 | 1 | 6 | (86) |
| Sepur, Cabahonito | 28 | 17 | 11 | (39) | 2 | 1 | 1 | (50) |
| Boloma, Santa Fe | 41 | 15 | 26 | (65) | 6 | 2 | 4 | (67) |
| TOTAL | 298 | 109 | 189 | (65) | 66 | 20 | 46 | (70) |

**Table 9. Degree of coverage accomplished for the selected sample and number of serum and breast milk specimens examined.**

| Survey period | Families in sample | | No. serum specimens from: | | | No. milk specimens from: | | |
|---|---|---|---|---|---|---|---|---|
| | Registered[1] and dietary | Attended Clin. Exam. | Sample Children | Other Children | Total | Sample Women | Other Women | Total |
| Oct-Nov 1975 | 358 | 263 | 401 | 148 | 549 | 121 | 162 | 283 |
| Apr-May 1976 | 361 | 269 | 367 | 219 | 586 | 108 | 204 | 312 |
| Oct-Nov 1976 | 360 | 253 | 377 | 268 | 645 | 89 | 148 | 237 |
| Apr-May 1977 | 360 | 248 | 358 | 316 | 674 | 80 | 209 | 289 |
| Oct-Nov 1977 | 355 | 203 | 324 | 397 | 721 | 74 | 180 | 254 |
| TOTAL | 1794 | 1226 | 1827 | 1348 | 3175 | 472 | 903 | 1375 |

[1] All families registered were interviewed by the Dietary Team.

team visited the homes, which meant that the families did not have to attend a central survey place in order to participate.

The strategy defined for the biochemical and clinic-anthropometric investigations was different. In this case, as had been described under "Methodology," the mothers or another adult person had to come to the clinical examination center and bring the preschool children who had previously been selected and registered for the study. A number of factors mainly of social nature, like excessive work of the mother at home or refusal, prevented some children from attending the clinical examination center on the only day that the clinical team was present at the village. This fact determined that not all the 30 families previously registered participated in the examination. The number of families in the original sample in each village that actually participated in each one of the survey periods is given in Table 9. It is noteworthy, however, that the number of preschool children belonging to these 360 families preselected according to the sampling framework surpassed the figure of 300 preschool children per survey considered adequate according to the statistical principles used.

An interesting phenomenon was the very important number of families who attended the clinical examination center on a voluntary basis without pertaining to the main sample, requested to be clinically examined, and also offered on a voluntary basis a sample of blood from their preschool age children or a sample of milk if they were lactating women. The number of preschool children from the village who were examined in this "other children" category as well as the number of milk specimens collected from lactating women outside the sample are also given in Table 9.

This raised the question as to whether the subjects examined as part of the sample group represented the same or a different universe from the ones who came on a voluntary basis. In order to determine that, a strict statistical approach was used to compare some of the more quantitative results characterizing both groups in a separate manner. The analysis referred to above indicated that there was no difference between the preselected and the other groups. Details of the statistical data to reach this conclusion are given in Tables 10, 11, and 12. For the analysis of the biochemical data, therefore, all the samples collected were

pooled and studied as only one group.

For the study of liver reserves, a total of 770 autopsy specimens were obtained throughout the evaluation period. The number of samples collected permitted to group them by trimester periods, beginning October 1975, that is, before the beginning of the fortification. Due to administrative anomalies, the collection of samples was very scanty during April-June 1977 (only 10 cases), and it was decided to merge them with the data of the following three-month period. The number of cases distributed by the consecutive time-periods appear in Table 13 and in the corresponding tables and figures in the section on "Results." It can be seen in Table 13 that the distribution of the cases by age-groups was rather even, with the exception of the 20-24 and 25-29 years of age that provided the highest numbers.

**Table 10. Comparison between serum retinol data of the preschool children for the "sample" and "out-of-sample" cases.**

| | No. | Percent of cases by categories of serum retinol levels in µg/100 ml | | | | | "Chi²" |
|---|---|---|---|---|---|---|---|
| | | <10 | 10-19 | 20-29 | 30-39 | ≥40 | |
| Sample children | 1812 | 1.0 | 10.6 | 31.2 | 38.2 | 19.0 | 2.74 (N.S.) |
| Out-of-sample | 1349 | 1.2 | 11.0 | 32.2 | 37.3 | 18.3 | |

The same test was applied to each survey period separately. All comparisons showed that the sample did not differ statistically from the out-of-sample group.

**Table 11. Comparison between breast milk retinol data for the "sample" and "out-of-sample" cases.**

| | No. | Percent of cases by categories of breast-milk retinol in µg/100 ml | | | | | | | | | | | "Chi²" |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | < 10 | 10-19 | 20-29 | 30-39 | 40-49 | 50-59 | 60-69 | 70-79 | 80-89 | 90-99 | ≥100 | |
| Sample women | 472 | 7.4 | 17.4 | 21.7 | 16.1 | 14.9 | 8.9 | 4.0 | 2.8 | 2.3 | 1.3 | 3.2 | 5.28 (N.S.) |
| Out-of-sample | 903 | 5.4 | 17.6 | 21.6 | 17.4 | 13.5 | 8.5 | 5.0 | 2.9 | 1.6 | 1.7 | 4.4 | |

The same test was applied to each survey period separately. All comparisons showed that the sample did not differ significantly from the out-of-sample groups.

**Table 12. Comparison between biochemical data for the "sample" and out-of-sample" cases.**

| | Serum retinol (µg/100 ml) | | | | Breast milk-retinol (µg/100 ml) | | | |
|---|---|---|---|---|---|---|---|---|
| | n | $\bar{x}$ | SD | "t" | n | $\bar{x}$ | SD | "t" |
| Sample cases | 1822 | 31.8 | 9.87 | 0.53 (NS) | 472 | 38.8 | 35.57 | 0.47 (NS) |
| Out-of-sample | 1349 | 31.6 | 10.59 | | 903 | 39.7 | 29.46 | |

The same "t-test" was applied to each survey period. All comparisons showed that the sample did not differ significantly from the out-of-sample group, except for breast-milk of survey No. 3 (Oct-Nov 1976) which gave a difference significant at the 5% level.

**Table 13. Numbers of liver specimens by age and trimester periods.**

| Age (years) | Oct-Dec 75 | Jan-Mar 76 | Apr-Jun 76 | Jul-Sep 76 | Oct-Nov 76 | Jan-Mar 77 | Apr-Sep 77* | All periods |
|---|---|---|---|---|---|---|---|---|
| 0-4 | 4 | 8 | 5 | 20 | 8 | 7 | 4 | 56 |
| 5-9 | 3 | 2 | 3 | 13 | 3 | 6 | 4 | 34 |
| 10-14 | 5 | 1 | 6 | 7 | 6 | 6 | 5 | 36 |
| 15-19 | 6 | 5 | 8 | 9 | 10 | 12 | 12 | 62 |
| 20-24 | 7 | 4 | 14 | 19 | 14 | 18 | 26 | 102 |
| 25-29 | 12 | 9 | 14 | 22 | 16 | 15 | 17 | 105 |
| 30-34 | 4 | 4 | 9 | 11 | 9 | 11 | 10 | 58 |
| 35-39 | 8 | 7 | 13 | 6 | 8 | 13 | 8 | 63 |
| 40-44 | 5 | 2 | 8 | 9 | 4 | 6 | 8 | 42 |
| 45-49 | 4 | 6 | 7 | 14 | 3 | 3 | 8 | 45 |
| 50-54 | 4 | 1 | 3 | 4 | 6 | 8 | 4 | 30 |
| 55-59 | 4 | 5 | 6 | 5 | 5 | 8 | 2 | 35 |
| 60-64 | 3 | 1 | 7 | 4 | 5 | 5 | 5 | 30 |
| 65-69 | 5 | 5 | 5 | 2 | 5 | 5 | 4 | 31 |
| 70-74 | 4 | 2 | 4 | 5 | 5 | 0 | 5 | 25 |
| 75- > | 2 | 4 | 0 | 2 | 4 | 2 | 1 | 16 |
| All ages | 80 | 67 | 112 | 152 | 111 | 145 | 123 | 770 |

* Semester

## Dietary Study

In view of the objectives of the evaluation project and of the scope of the present report the results presented in this section will emphasize: a) the dietary pattern of the population studied, with reference to those characteristics that are relevant to vitamin A nutrition, b) the intake of retinol equivalents (in µg/capita/day) from natural food sources only, and the estimated retinol intake from the consumption of fortified sugar; c) the extent to which the nutritional needs of the target population (per cent adequacy of the intake of retinol equivalents) were improved by the fortification.

The information obtained on specific foods consumed by families confirms previous studies in this type of population (7).

The dietary pattern with respect to energy and retinol is as shown in Table 14, where those food items which are sources of vitamin A (retinol or carotene) can be identified. In that table, the per cent contribution of the main vitamin A food sources is given for each survey period. It can be seen that without fortification (October-November 1975), vegetables are the main contributors to the intake of vitamin A (as carotenes), meats and dairy products follow. Despite their very high contribution to energy intake, cereals contribute relatively little to the vitamin A value of the diet. This is explained by the fact that essentially all the "cereal" group in the population studied is represented by white corn.

When the surveys carried after fortification started (April-May 1976 through Octo-

**Table 14. Percent contribution of average diets to energy and vitamin A intake, Guatemala, 1975-1977.**

| Foods | Oct-Nov 75 | | Apr-May 76 | | Oct-Nov 76 | | Apr-May 77 | | Oct-Nov 77 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Cal. | Ret. | Cal. | Ret. | Cal. | Ret. | Cal. | Ret. | Cal. | Ret. |
| | - Percentages - | | | | | | | | | |
| Milk products | 3 | 14 | 2 | 3 | 2 | 4 | 2 | 3 | 3 | 5 |
| Eggs | 1 | 5 | 1 | 3 | 1 | 2 | 1 | 2 | 1 | 2 |
| Meats | 3 | 18 | 3 | 0 | 3 | 0 | 3 | 12 | 2 | 0 |
| Beans | 10 | 0 | 11 | 0 | 10 | 0 | 10 | 0 | 8 | 0 |
| Vegetables | 4 | 51 | 1 | 10 | 2 | 12 | 1 | 7 | 2 | 10 |
| Fruits | 0 | 1 | 1 | 5 | 1 | 0 | 1 | 7 | 1 | 0 |
| Bananas & plantains | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Starchy roots & tubers | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Cereal products | 65 | 9 | 68 | 6 | 69 | 5 | 65 | 4 | 68 | 4 |
| Sugar | 5 | 0 | 9 | 73 | 9 | 74 | 10 | 60 | 11 | 74 |
| Fats & oil | 2 | 0 | 3 | 0 | 2 | 0 | 3 | 0 | 2 | 0 |
| Miscellaneous | 1 | 0 | 1 | 0 | 1 | 2 | 1 | 3 | 1 | 2 |

**Table 15. Consumption of white and raw sugar ("panela") in the rural area of Guatemala, 1975-1977 (in grams per day).**

| Community | Oct-Nov 75 | | Apr-May 76 | | Oct-Nov 76 | | Apr-May 77 | | Oct-Nov 77 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Sugar | Panela | Sugar | Panela | Sugar | Panela | Sugar | Panela | Sugar | Panela |
| El Barreal | 37 | - | 38 | - | 45 | - | 54 | 2 | 59 | - |
| Santa María | 51 | - | 47 | - | 46 | - | 37 | 1 | 53 | - |
| San Juan | 31 | 10 | 36 | 7 | 68 | 1 | 48 | 6 | 47 | 14 |
| El Jícaro | 45 | 4 | 39 | 7 | 58 | 4 | 61 | 3 | 55 | 11 |
| Buena Vista | 21 | 10 | 19 | 5 | 32 | 4 | 24 | 14 | 31 | 14 |
| San Rafael | 14 | 17 | 28 | 6 | 27 | 9 | 33 | 4 | 42 | 3 |
| Saquitacaj | 24 | 8 | 32 | 3 | 37 | 3 | 17 | 9 | 21 | 10 |
| La Libertad | 73 | 1 | 40 | 9 | 51 | 2 | 57 | 2 | 49 | 3 |
| Cubulco | 7 | 13 | 29 | 19 | 41 | 6 | 49 | 17 | 37 | 14 |
| San Carlos | 30 | 1 | 43 | 2 | 42 | - | 50 | 4 | 40 | 1 |
| Cahaboncito | 22 | - | 19 | - | 19 | - | 21 | - | 30 | - |
| Santa Fe | 56 | - | 32 | - | 47 | - | 52 | - | 71 | - |
| Weighted averages | 35 | 5 | 34 | 5 | 43 | 2 | 42 | 5 | 45 | 6 |

ber–November 1977) are analyzed, the marked effect of the introduction of the "new" source of retinol (fortified sugar) can clearly be observed. Sugar becomes by and large the main contributor to the preformed retinol content of the diet, reaching per cent contribution figures higher than all food sources together, before the introduction of fortified sugar. Because of the fortification programs, sugar has become a food source of retinol equivalents. Therefore, it was essential to estimate its consumption by the population. Table 15 summarizes these data for each of the five survey periods. Within the limits of error of the dietary field studies as conducted, the data are considered rather consistent, although an apparently sudden increase is observed beginning at the second survey of 1976. By clear policy, predetermined efforts were made to avoid any type of promotion or stimulus for greater consumption of sugar after this food item became fortified. Therefore, the increased consumption observed remains unexplained. The specific average intake of sugar for the 1–5-year old children (indicator age-group for the evaluation) is given in Table 16, showing that they consumed about 77 per cent of the family average, contributing 330 μg of retinol equivalents per child per day. The results are very similar to those of previous studies carried out in rural Guatemala in 1965 (25).

Of central relevance to the interpretation of the evaluation data is the estimated intake of vitamin A at the level of the population studied. Table 17 presents the average per capita daily intake of retinol equivalents found at each survey period. After the prefortification survey (baseline), the contribution of fortified sugar has been added. It is evident that sugar as a new source of vitamin A tripled the retinol equivalents provided by the natural food sources.

The comparison of these intake figures with the recommended allowances (2) adjusted for age, sex, and physiologic state of the family members gives rise to the estimates of adequacy of intake at the family level, that is, the extent to which each family unit surveyed was satisfying its vitamin A needs. Table 18 summarizes the distribution of the families by categories of adequacy. The notorious and highly significant effect of the fortification ($Chi^2$ = 90.67; critical value for P = 0.001 = 18.47) essentially reversed the distribution. While 83 per cent of the families had retinol

**Table 16. Consumption of sugar per child per day in the rural area of Guatemala, 1977.**

| | Apr–Sep grams | Oct–Nov grams |
|---|---|---|
| Average | 34 | 36 |
| Maximum | 68 | 50 |
| Minimum | 10 | 11 |

Total number of children: 300 in each period.

**Table 17. Daily per capita intake of retinol equivalents[1], Guatemala, 1975-1977.**

| Survey Period | From natural food sources | From fortified sugar[2] | Total |
|---|---|---|---|
| Oct-Nov 1975 (Basal) | 221 | 0 | 221 |
| Apr-May 1976 | 178 | 336 | 514 |
| Oct-Nov 1976 | 198 | 425 | 623 |
| Apr-May 1977 | 251 | 419 | 670 |
| Oct-Nov 1977 | 182 | 445 | 627 |

[1] In μg

[2] At a calculated level of fortification = 10 μg retinol/g sugar

**Table 18. Distribution of families by percent adequacy of vitamin A intake, Guatemala, 1975-1977.**

PART A. Sugar without vitamin A

| Survey period | No. of families surveyed | Level of adequacy of vitamin in diet (percent of adequacy) | | | | |
|---|---|---|---|---|---|---|
| | | <25 | 25-49 | 50-74 | 75-99 | 100> |
| | | - Percent of families at each level - | | | | |
| Oct-Nov 1975 (basal) | 355 | 60 | 23 | 6 | 4 | 7 |
| Apr-May 1976 | 360 | 63 | 22 | 7 | 3 | 5 |
| Oct-Nov 1976 | 360 | 54 | 27 | 10 | 4 | 5 |
| Apr-May 1977 | 360 | 43 | 25 | 14 | 7 | 11 |
| Oct-Nov 1977 | 356 | 51 | 24 | 14 | 5 | 6 |

PART B. Sugar with vitamin

| | | | | | | |
|---|---|---|---|---|---|---|
| Oct-Nov 1975 | 355 | - | - | - | - | - |
| Apr-May 1976 | 360 | 13 | 15 | 22 | 15 | 35 |
| Oct-Nov 1976 | 360 | 8 | 12 | 14 | 17 | 49 |
| Apr-May 1977 | 360 | 9 | 10 | 15 | 13 | 53 |
| Oct-Nov 1977 | 356 | 8 | 9 | 15 | 13 | 55 |

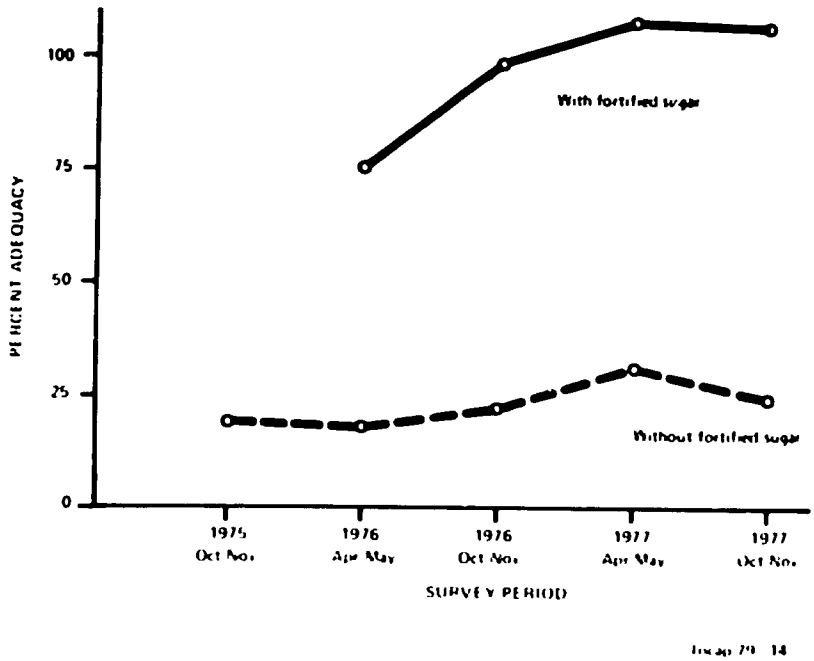


**Figure 3. Changes in the 50th percentile of intake of retinol equivalents without and with the contribution of fortified sugar.**

intakes lower than 50 per cent adequacy before the fortification began (October-November 1975). 83 per cent of them reached adequacies of 50 per cent or higher by October-November 1977 as a result of the fortification program. The progression of the 50th percentile adequacy values, illustrated in Figure 3, further documents this improvement in the vitamin A dietary situation of the population studied.

## Biochemical Results

*Blood serum retinol.* It has previously been explained in this report that the blood serum retinol concentration of rural children of preschool age (1-5 years) was defined as a main indicator for the evaluation of the nutritional effect of the program of fortification. The reasons for this decision as well as the approach to the interpretation of the results have been given.

Table 19 presents the changes in the distribution of retinol values in categories of adequacy. A decrease in the percentage of children with values lower than 10 μg/100 ml ("deficient") was observed. This trend is more clearly shown by Figure 4. The proportion of samples between 10 and 19 μg/100 ml ("low") also decreased, although the lowest figure was obtained in October-November 1976. Considering together the values below 20 μg/100 ml, the 21.5 per cent of these values before the program was reduced to 9.2 per cent after two years of fortification.

The changes in distribution of the values described are highly significant ($Chi^2$ = 116.55, P < 0.001). When comparing the baseline distribution (October-November 1975) specifically with the third survey

**Table 19. Blood serum retinol levels in preschool children, Guatemala, 1975-1977.**

| Survey period | No. Cases | Percent of cases by categories of serum retinol level (µg/100 ml) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | <10 | | 10-19 | | 20-29 | | ≥30 | |
| | | n | (%) | n | (%) | n | (%) | n | (%) |
| Oct-Nov 1975 | 543 | 18 | (3.3)[1] | 100 | (18.2) | 189 | (34.8) | 232 | (44.1) |
| Apr-May 1976 | 585 | 6 | (1.0) | 77 | (13.1) | 205 | (35.5) | 295 | (50.4) |
| Oct-Nov 1976 | 644 | 2 | (0.3) | 31 | (4.8) | 165 | (25.6) | 447 | (69.3) |
| Apr-May 1977 | 676 | 6 | (0.9) | 69 | (10.2) | 189 | (28.0) | 410 | (60.9) |
| Oct-Nov 1977 | 721 | 2 | (0.3) | 64 | (8.9) | 260 | (36.1) | 395 | (54.6) |

[1]Figures in parentheses = percent of cases

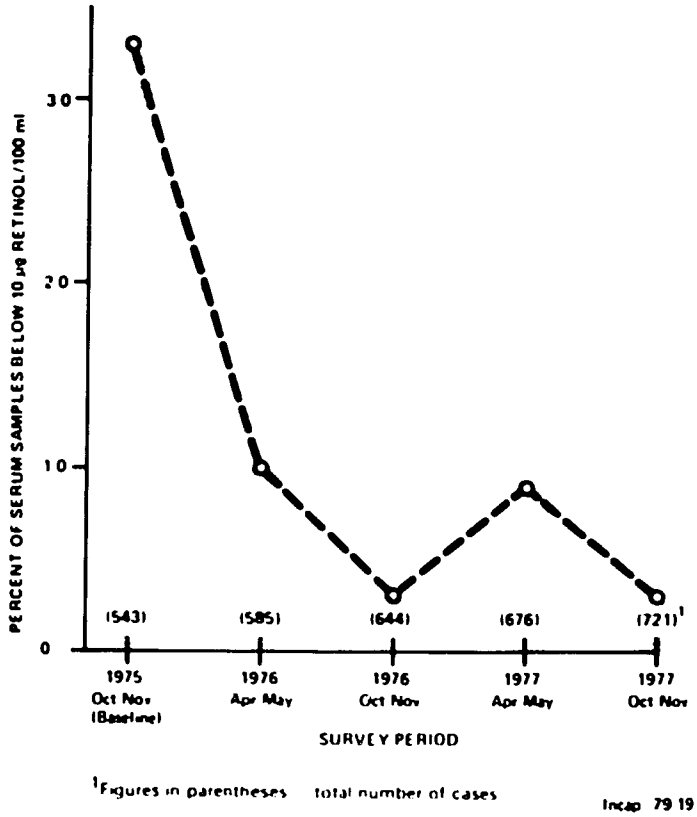


**Figure 4. Decrease in the percent of children with "deficient" serum retinol levels.**

(October-November 1976) a highly significant difference was again obtained ($Chi^2 = 104.72$; $P < 0.001$). Despite a tendency for the distribution of values during the fifth survey (October-November 1977) to regress somewhat, a highly significant difference with the prefortification values was still shown ($Chi^2 = 16.23$; $P < 0.001$).

It was considered important to examine the distribution data for the individual communities, as given in Table 20. It can be noted that, regardless of the initial per cent of children in the "deficient" category (< 10 μg/100 ml), all the communities except two had no cases in this "deficient" range by October-November 1977. Even in these two communities, a marked improvement could be observed (La Libertad 3.3 to 1.4 per cent; Cubulco 4.3 to 1.3 per cent). Regarding the serum retinol values between 10 and 19 μg/100 ml ("low"), 11 of the communities showed a decrease, although to varying degrees. One community (Saquitacaj) clearly did not improve as judged by this biochemical indicator. Another evident fact is that there is a general tendency for the results corresponding to October-November 1976 to be better than for 1977. A possible explanation for this tendency to regress will be discussed later.

The International Vitamin A Consultative Group (IVACG) in its *Guidelines for the Eradication of Vitamin A Deficiency and Xerophthalmia* (*16*) has recommended that: "For the purpose of program evaluation it is important to look at population distribution curves for serum vitamin A values." This specific recommendation has been applied to the data from the present study, and the results are presented in Figures 5 and 6. These distribution curves make evident with obvious clarity the very important changes which occurred in the group of rural children during the two years of sugar fortification. In October-November 1975, that is, just before the national program started, the distribution curve was obviously abnormal, as it showed two peaks. The higher peak to the left indicated the existence of a distinguishable sub-group of children with a more inadequate vitamin A nutritional status or, in other words, a more vulnerable sector of the population. After only 4.5 months of fortification, the obvious impact of the higher intake of retinol is shown by the distribution obtained during the second survey ($P < 0.025$). The peak representing the sub-group with the lowest serum retinol values is disappearing, remaining only a hump on the left slope of the curve. By October-November 1976 two very significant epidemiologic changes had occurred: a) the distribution curve had been shifted to the right ($P < 0.001$); and, b) the shape of the curve had become essentially normal. As the evaluation continued during 1977, one notices the tendency to regress that was already pointed out. The curve for the fourth survey (April-May 1977) does not differ significantly from the one before (October-November 1977). However, by the last survey (October-November 1977), one can see the tendency for the curve to become somewhat abnormal again with a slight hump on the left slope. Ultimately, however, there is still a highly significant difference between the prefortification baseline distribution curve of retinol serum values and that obtained at the last survey ($Chi^2 = 47.04$; $P < 0.001$).

In spite of the cross-sectional design used in the study, due to the small size of the communities surveyed many children were randomly sampled in more than one survey. This has provided the opportunity to evaluate the impact of the fortification on a longitudinal basis in terms of changes in serum retinol in the same child. The approach used was as follows: comparisons were made between consecutive surveys of the serum retinol levels of the children who had a pair of consecutive retinol determinations such as survey I versus survey II,

**Table 20. Blood serum retinol levels in preschool children for each of the communities, Guatemala, 1975-1977.**

| Community and survey period | N | Percent of cases by categories of serum retinol level (μg/100 ml) | | | |
|---|---|---|---|---|---|
| | | <10 | 10-19 | 20-29 | ≥30 |
| El Barreal: | | | | | |
| Oct-Nov 75 (basal) | 51 | 0.0 | 29.4 | 35.3 | 35.3 |
| Apr-May 76 | 58 | 0.0 | 17.2 | 22.4 | 60.4 |
| Oct-Nov 76 | 69 | 0.0 | 10.1 | 33.3 | 53.6 |
| Apr-May 77 | 71 | 0.0 | 2.8 | 11.3 | 83.1 |
| Oct-Nov 77 | 72 | 0.0 | 5.6 | 30.6 | 63.9 |
| Santa María: | | | | | |
| Oct-Nov 75 | 45 | 8.9 | 20.0 | 42.2 | 28.8 |
| Apr-May 76 | 59 | 0.0 | 16.9 | 47.5 | 33.9 |
| Oct-Nov 76 | 71 | 0.0 | 14.1 | 31.0 | 54.9 |
| Apr-May 77 | 72 | 1.4 | 15.3 | 43.1 | 38.9 |
| Oct-Nov 77 | 98 | 0.0 | 7.1 | 45.9 | 46.9 |
| San Juan: | | | | | |
| Oct-Nov 75 | 51 | 2.0 | 23.5 | 27.5 | 47.1 |
| Apr-May 76 | 37 | 0.0 | 8.1 | 43.2 | 48.6 |
| Oct-Nov 76 | 33 | 0.0 | 0.0 | 21.2 | 78.8 |
| Apr-May 77 | 29 | 0.0 | 0.0 | 20.7 | 79.3 |
| Oct-Nov 77 | 56 | 0.0 | 16.1 | 30.4 | 53.5 |
| El Jícaro: | | | | | |
| Oct-Nov 75 | 40 | 5.2 | 15.0 | 45.0 | 35.0 |
| Apr-May 76 | 58 | 1.7 | 22.4 | 50.0 | 25.9 |
| Oct-Nov 76 | 56 | 0.0 | 0.0 | 21.4 | 78.6 |
| Apr-May 77 | 69 | 0.0 | 2.9 | 20.3 | 76.8 |
| Oct-Nov 77 | 55 | 0.0 | 10.9 | 54.5 | 34.6 |

**Table 20. Blood serum retinol levels in preschool children for each of the communities, Guatemala, 1975-1977 (*continued*).**

| Community and survey period | N | Percent of cases by categories of serum retinol level (μg/100 ml) | | | |
|---|---|---|---|---|---|
| | | <10 | 10–19 | 20–29 | ≥30 |
| Buena Vista: | | | | | |
| Oct-Nov 75 | 39 | 5.1 | 10.3 | 38.5 | 46.1 |
| Apr-May 76 | 35 | 5.7 | 20.0 | 45.7 | 28.6 |
| Oct-Nov 76 | 37 | 0.0 | 0.0 | 24.3 | 75.7 |
| Apr-May 77 | 64 | 0.0 | 20.3 | 21.9 | 57.8 |
| Oct-Nov 77 | 73 | 0.0 | 2.7 | 28.8 | 68.5 |
| San Rafael: | | | | | |
| Oct-Nov 75 | 48 | 6.3 | 8.3 | 16.7 | 68.7 |
| Apr-May 76 | 30 | 0.0 | 10.0 | 43.3 | 46.7 |
| Oct-Nov 76 | 26 | 3.8 | 0.0 | 11.5 | 84.7 |
| Apr-May 77 | 33 | 0.0 | 6.1 | 18.2 | 75.7 |
| Oct-Nov 77 | 18 | 0.0 | 5.4 | 33.3 | 61.1 |
| Saquitacaj: | | | | | |
| Oct-Nov 75 | 22 | 0.0 | 9.1 | 36.4 | 54.5 |
| Apr-May 76 | 54 | 1.9 | 18.5 | 25.9 | 53.7 |
| Oct-Nov 76 | 66 | 1.5 | 4.5 | 24.2 | 69.8 |
| Apr-May 77 | 48 | 4.2 | 18.8 | 31.3 | 45.7 |
| Oct-Nov 77 | 18 | 0.0 | 11.1 | 50.0 | 38.9 |
| La Libertad: | | | | | |
| Oct-Nov 75 | 30 | 3.3 | 23.3 | 13.3 | 60.1 |
| Apr-May 76 | 47 | 0.0 | 10.6 | 36.2 | 53.2 |
| Oct-Nov 76 | 44 | 0.0 | 4.5 | 25.0 | 70.5 |
| Apr-May 77 | 46 | 2.2 | 6.5 | 28.3 | 63.0 |
| Oct-Nov 77 | 72 | 1.4 | 2.8 | 29.2 | 66.8 |

**Table 20. Blood serum retinol levels in preschool children for each of the communities, Guatemala, 1975–1977 (*continued*).**

| Community and survey period | N | Percent of cases by categories of serum retinol level (µg/100 ml) | | | |
|---|---|---|---|---|---|
| | | <10 | 10–19 | 20–29 | ≥30 |
| Cubulco: | | | | | |
| Oct–Nov 75 | 46 | 4.3 | 26.1 | 32.6 | 37.0 |
| Apr–May 76 | 45 | 0.0 | 8.9 | 35.6 | 55.6 |
| Oct–Nov 76 | 62 | 0.0 | 3.2 | 29.0 | 67.8 |
| Apr–May 77 | 54 | 1.9 | 11.1 | 33.3 | 53.7 |
| Oct–Nov 77 | 76 | 1.3 | 15.8 | 46.1 | 36.9 |
| San Carlos: | | | | | |
| Oct–Nov 75 | 59 | 1.7 | 22.0 | 40.7 | 35.6 |
| Apr–May 76 | 51 | 3.9 | 7.8 | 25.5 | 62.8 |
| Oct–Nov 76 | 48 | 0.0 | 2.1 | 16.7 | 81.3 |
| Apr–May 77 | 52 | 0.0 | 1.9 | 17.3 | 80.7 |
| Oct–Nov 77 | 44 | 0.0 | 11.4 | 36.4 | 52.2 |
| Ca abonerito: | | | | | |
| Oct–Nov 75 | 45 | 4.4 | 22.2 | 44.4 | 28.9 |
| Apr–May 76 | 60 | 0.0 | 8.3 | 36.7 | 55.0 |
| Oct–Nov 76 | 69 | 0.0 | 7.2 | 29.0 | 63.8 |
| Apr–May 77 | 72 | 1.4 | 18.1 | 47.2 | 33.4 |
| Oct–Nov 77 | 75 | 0.0 | 14.7 | 30.7 | 54.7 |
| Santa Fe: | | | | | |
| Oct–Nov 75 | 73 | 0.0 | 8.2 | 35.6 | 56.1 |
| Apr–May 76 | 52 | 0.0 | 5.8 | 21.2 | 73.1 |
| Oct–Nov 76 | 64 | 0.0 | 1.5 | 25.0 | 73.5 |
| Apr–May 77 | 64 | 0.0 | 10.8 | 32.8 | 56.4 |
| Oct–Nov 77 | 64 | 0.0 | 4.7 | 23.4 | 71.9 |

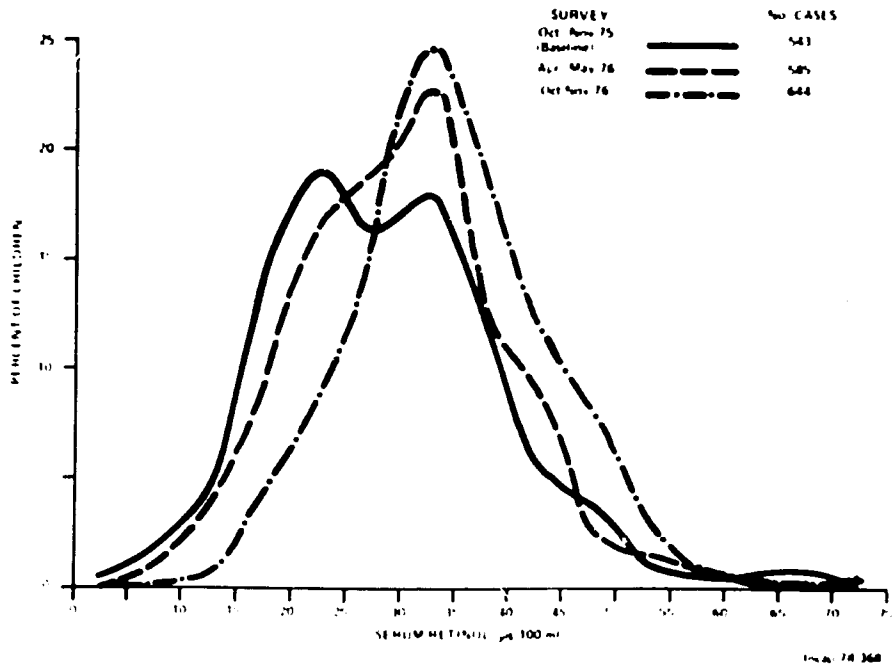


Figure 5. Effect of sugar fortification with vitamin A on the distribution of serum retinol levels of rural preschool children, 1975-1976.

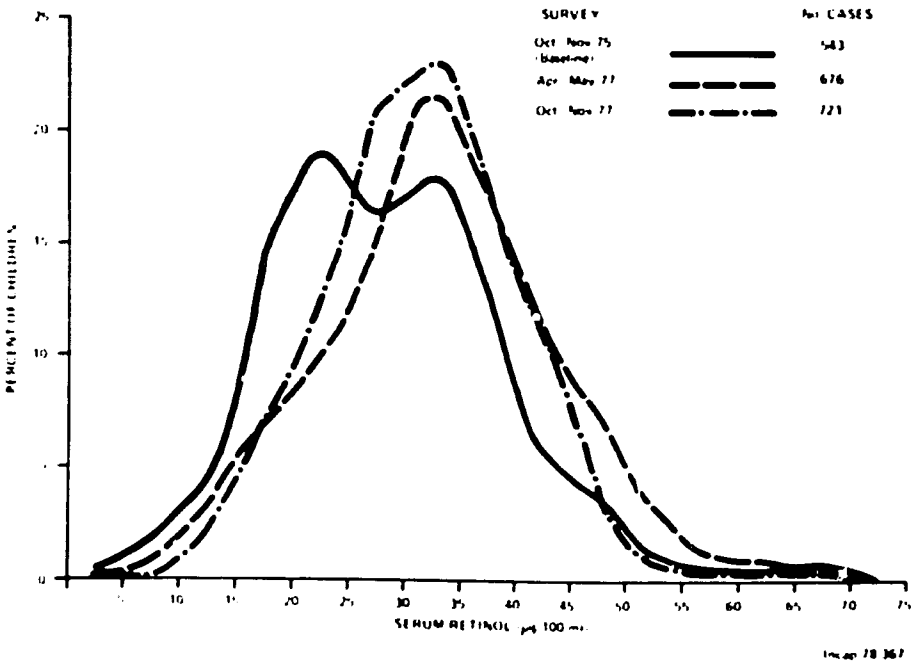


Figure 6. Effect of sugar fortification with vitamin A on the distribution of serum retinol levels of rural preschool children, 1975-1977.

survey II versus III, etc. In addition, in order to study the effect of a more prolonged intervention period, comparisons were also made between survey I (prefortification October-November 1975) and survey III (one year of fortification October-November 1976) and between survey I and survey V (two years of fortification October-November 1977). In each group of pairs studied, initial serum retinol levels were classified in categories of < 10, 10 to < 20 and ≥20 μg/100 ml. Children who fell in these categories were examined in terms of their change in serum retinol through time. The magnitude of this change in retinol was also categorized in terms of being < 5, 5 to 9, 10 to 14, 15 to 19, and ≥20 μg/100 ml.

In general, the pairs of surveys compared showed the same positive effect of vitamin A fortification on serum retinol levels, particularly in children who initially had low levels. For simplicity and because of their special public health importance, the results from those children with initial serum retinol < 10 and between 10 and < 20 μg/100 ml are presented. Furthermore, since the results obtained for all the comparisons made were similar, Table 21 includes analysis of survey I (baseline) versus survey III and survey I versus survey V. Both comparisons represent, respectively, the effect of one and two years of vitamin A fortification.

Due to the random nature of the sampling procedure used in each of the five cross-sectional studies, the number of children with a pair of determinations varied for each comparison unit. There was a total of 96 children sampled both in surveys I and III, among whom there were 18 with initial serum retinol levels < 20 μg/100 ml in October-November 1975 (survey I). The changes observed in serum retinol in these 18 children after one year of fortification are presented in Part A of Table 21. Initially there was only one child with a retinol value less than 10 μg/100 ml. One year later (October-November 1976), this child had shown an increase from 7.0 to 16.5 μg/100 ml. All the 17 children who had retinol levels between 10 and 20 μg/100 ml in survey I showed increases in this parameter one year later as follows: three children by < 5 μg; two by 5 to 9 μg; three by 10 to 14 μg; five by 15 to 19 μg; and four by ≥20 μg/100 ml. The average serum retinol value for these 18 children was 16.2 ± S.D. 2.9 in the initial survey and 30.2 ± S.D. 9.7 in survey III, an increase which was highly significant (P < 0.0001).

A total of 72 children were compared between October-November 1975 (survey I) and October-November 1977 (survey V), of whom one child had initially serum retinol < 10 μg and 15 between 10 and < 20 μg/100 ml. The analysis of the longitudinal changes experienced by these children is presented in part B of Table 21. The child with initial serum retinol < 10 μg/100 ml increased from 8.4 to 22.9 μg/100 ml. Of the 15 children between 10 and < 20 μg/100 ml, two experienced a decrease in their serum retinol; these decreases were both by less than < 10 μg/100 ml. In the other 13 children, the serum retinol was higher at survey V than at survey I, two by < 5 μg; five by 5 to 9 μg; three by 10 to 14 μg; two by 15 to 19 μg; and one by more than 20 μg/100 ml. The increase in the average serum retinol value for these 15 children was from 16.6 ± S.D. 3.0 in survey I to 26.1 ± S.D. 9.9 μg/100 ml in survey V, a difference which was highly significant (P < 0.0005).

These results clearly demonstrate the specific effectiveness of the program in elevating the level of serum retinol of precisely those children with undesirably reduced levels, reflecting their improvement in vitamin A nutritional status.

Because of the relatively large number of children studied in each survey period, it was possible to analyze the retinol serum values by one-year age groups, from 12 to 71

**Table 21. Longitudinal change in serum retinol of children with pre-fortification levels below 20 μg per 100 ml, Guatemala, 1975-1977.**

A. Changes from Oct-Nov 1975 (basal) to Oct-Nov 1976 (No. of pair comparisons = 96)

| Oct-Nov 1975 (basal) Serum level category (μg/100 ml) | No. | Direction of Change | Number of children found in Oct-Nov 76 whose serum retinol levels had increased or decreased by: <5 μg/100 ml | 5-9 μg/100 ml | 10-14 μg/100 ml | 15-19 μg/100 ml | ≥20 μg/100 ml | Total number of children whose serum retinol increased or decreased |
|---|---|---|---|---|---|---|---|---|
| <10 | 1 | Increased | 0 | 1 | 0 | 0 | 0 | 1 |
| | | Decreased | 0 | 0 | 0 | 0 | 0 | 0 |
| 10 to <20 | 17 | Increased | 3 | 2 | 3 | 5 | 4 | 17 |
| | | Decreased | 0 | 0 | 0 | 0 | 0 | 0 |

B. Changes from Oct-Nov 1975 (basal) to Oct-Nov 1977 (No. of pair comparisons = 72)

| Oct-Nov 1975 (basal) Serum level categroy (μg/100 ml) | No. | Direction of Change | Number of children found in Oct-Nov 77 whose serum retinol levels had increased or decreased by: <5 μg/100 ml | 5-9 μg/100 ml | 10-14 μg/100 ml | 15-19 μg/100 ml | ≥20 μg/100 ml | Total number of children whose serum retinol increased or decreased |
|---|---|---|---|---|---|---|---|---|
| <10 | 1 | Increased | 0 | 0 | 1 | 0 | 0 | 1 |
| | | Decreased | 0 | 0 | 0 | 0 | 0 | 0 |
| 10 to <20 | 15 | Increased | 2 | 5 | 3 | 2 | 1 | 13 |
| | | Decreased | 1 | 1 | 0 | 0 | 0 | 2 |

months of age. Table 22 presents these types of data. For simplicity and because the purpose of presenting the data in this manner was to test for the existence of an age effect on levels of serum retinol, only the results of the baseline survey and those of one year later are tabulated. It may be noted that within this age range there is no trend for the average values to increase consistently with age. Only the average value for the 12- to 23-month-olds during the basal survey (26.0 $\mu$g/100 ml) is lower ($t = 3.4$) than for the other age-groups in the same survey, but with the fortification this difference, although still significant ($t = 2.65$), tends to become smaller. The data so presented illustrate one additional important point: that the program has had a beneficial impact on the retinol serum levels of the preschool children regardless of age. In fact, it seems that the improvement in the youngest age-groups which initially had the lowest value was, if any, somewhat better. Whether this youngest age-group consumed relatively more fortified sugar cannot be determined from the present study, but it is unlikely. It is more reasonable to suppose that the 12- to 23-month-old children were still receiving the benefit of the vitamin A in breast milk which, as will be seen later, was increased by the consumption of fortified sugar by the lactating mothers.

*Breast milk retinol.* The methods and procedures to obtain the samples of milk from lactating women, as well as the rationale for selecting this parameter as an indicator of the nutritional impact of the sugar fortification program, have been presented previously in this report. A total of 1,275 samples, distributed rather equally among the five survey periods, were studied. The distribution of the breast milk retinol values obtained in each survey period after the beginning of the fortification was compared with that for the baseline survey. Figure 7 shows the trend for the values to move towards the right of the abscissae, reaching a maximum shift in April-May 1977. The blank area under the outline of the prefortification distribution points to the decrease in the per cent of milk samples with deficient levels of retinol. Statistical tests showed that the overall changes

**Table 22. Serum retinol values by age groups[1] ($\mu$g/100 ml).**

| Survey | | 12-23 | 24-35 | 36-47 | 48-59 | 60-71 |
|---|---|---|---|---|---|---|
| Oct-Nov 75 (Basal) | n | 101 | 97 | 130 | 107 | 93 |
| | $\bar{x}$ | 26.0 | 30.6 | 29.1 | 29.0 | 30.1 |
| | SD | 9.2 | 10.6 | 11.9 | 10.7 | 10.2 |
| Oct-Nov 76 | n | 107 | 132 | 117 | 132 | 135 |
| | $\bar{x}$ | 33.2 | 36.3 | 35.6 | 33.8 | 34.3 |
| | SD | 8.7 | 9.3 | 10.1 | 8.9 | 8.1 |

[1] In months

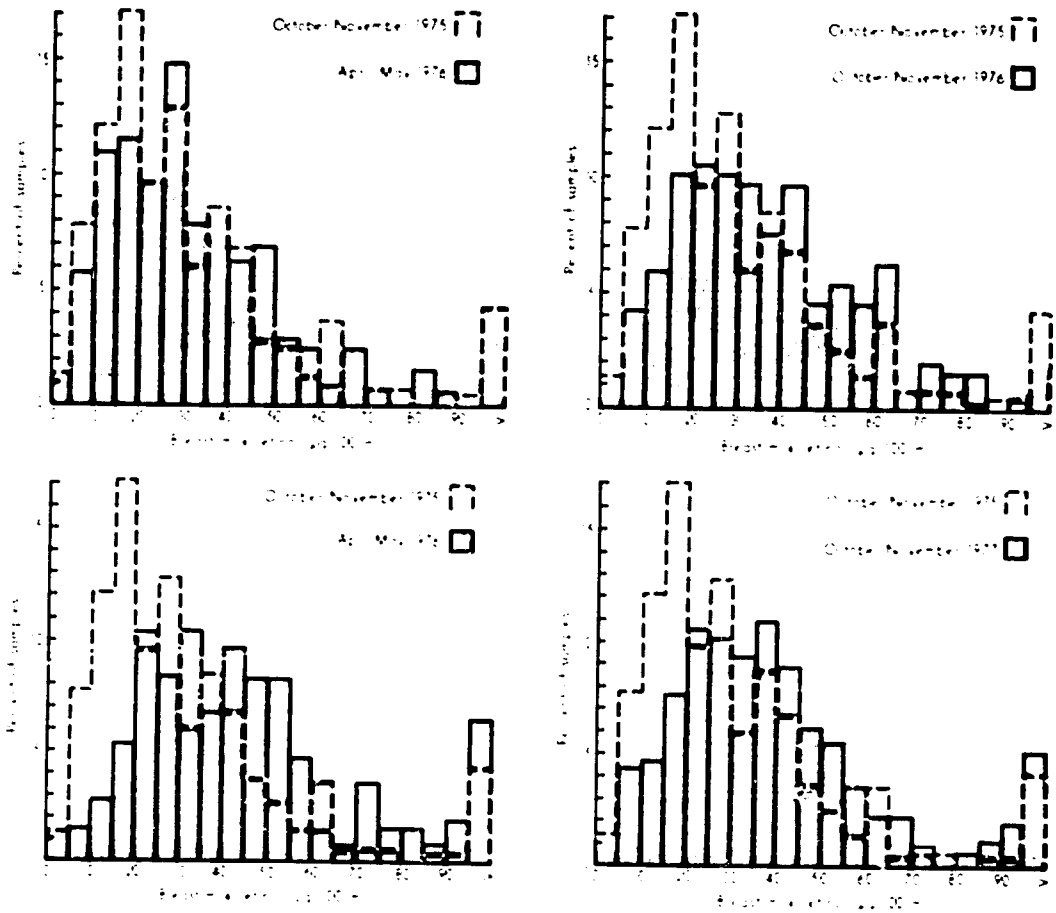

**Figure 7. Effect of fortification of sugar with vitamin A on the distribution of breast milk retinol.**

observed in the distribution were highly significant ($Chi^2$ = 133.07; P < 0.001). The pair comparisons between the baseline and survey III on the one hand ($Chi^2$ = 36.27) and the V survey on the other ($Chi^2$ = 40.43) also gave a highly significant different distribution (P < 0.001).

The changes in the first quartile, the median, and the third quartile are shown in Figure 8. Although the absolute increments do not seem very impressive, the relative improvement in the degree to which the breast fed infant fulfilled its recommended allowance for vitamin A may be epidemiologically very significant. In effect, if one takes the round figure of 600 ml day for breast milk intake from 0-6 months, an increase in concentration of 15 µg/100 ml represents 90 µg/d more for the infant. For "median" infants whose prefortification intake of retinol from breast milk could then be estimated as 153 µg of retinol day (25.5 µg/100 ml × 600 ml/100) the improvement in intake amounts to 60 per cent.

Still more relevant is the highly significant decrement ($Chi^2$ = 77.36; P < 0.001) in the per cent of milk specimens with less than 20 µg of retinol per 100 ml, value which

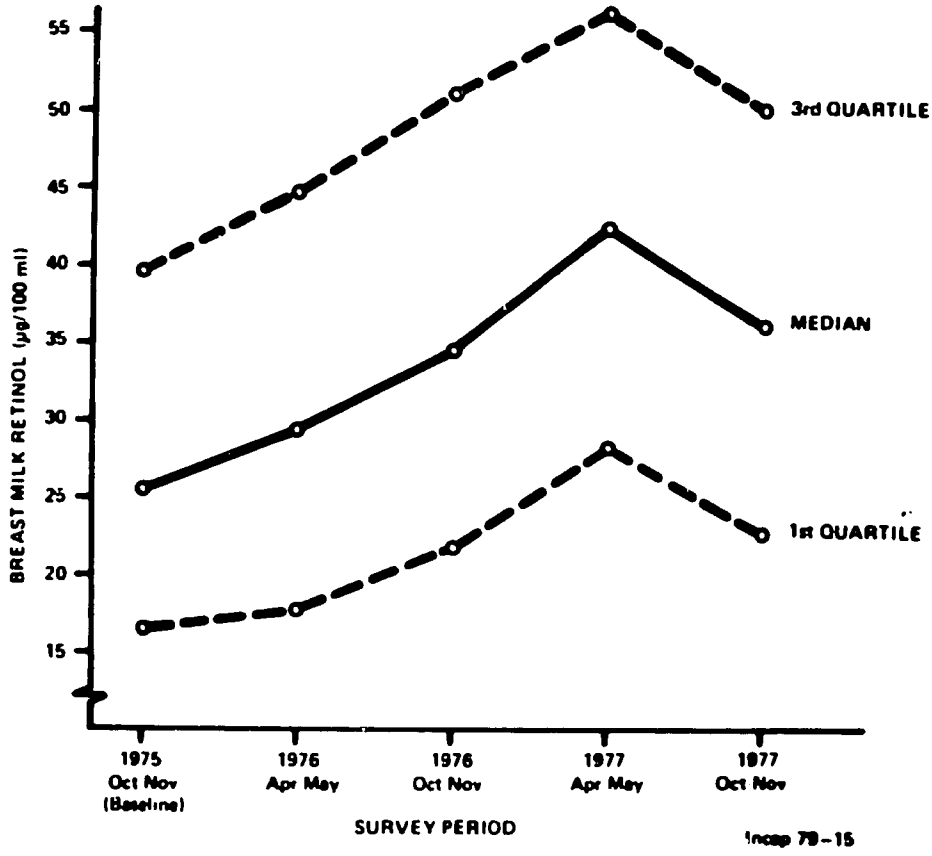


**Figure 8. Changes in the first, median, and third quartiles of breast milk retinol.**

represents about 40 per cent of the retinol content recognized by WHO as expected for mature human milk from well nourished, healthy lactating women (*18*). Figure 9 illustrates graphically this decrement in deficient level throughout the evaluation period. Because a slight increase in the cases with low retinol values was observed during the last survey, pair differences were tested between each individual survey and the prefortification distribution, showing a highly significant shift of values, both during October–November 1976 and during October–November 1977 ($Chi^2 = 20.11$ and 29.17, respectively; $P < 0.001$).

This analytic approach was also applied by periods of lactation, since it is recognized that the nutritional stress and response of the lactating women vary with the length and circumstances of lactation. The results are presented in Table 23. It is encouraging to observe that the beneficial effect of the consumption of fortified sugar is unquestionable for all periods, with an unexplained minor effect (N.S.) during the seventh to eighth lactation months. When one studies these data across the table, it is obvious that, before fortification, the worst situation appeared during the fifth and sixth months and the best during the first two months. This trend has been shown before during a study in a poor rural community in El Salvador (*7*). Epidemiologically, it probably reflects the fact that as lactation advances up to six months the vitamin A marginally nourished mother cannot maintain the relatively more adequate retinol content of the beginning of lacta-

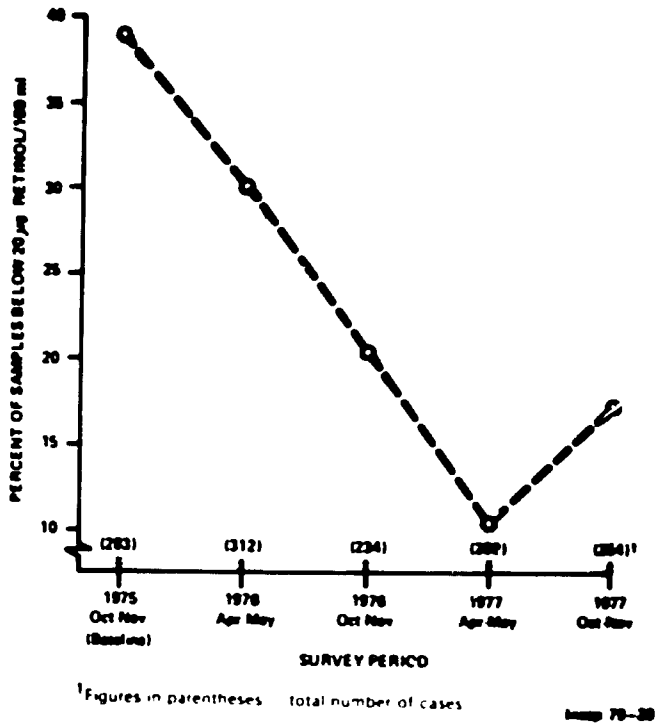


Figure 9. Decrease in the percent of breast milk samples with "deficient" retinol.

Table 23. Decrease in the percent of breast milk samples with less than 30 μg retinol/100 ml by period of lactation, Guatemala, 1975-1977.

| Survey period | Lactation period (months) | | | | | |
|---|---|---|---|---|---|---|
| | 0-2 (n=303) | 3-4 (n=216) | 5-6 (n=196) | 7-8 (n=195) | 9-10 (n=194) | ≥ 11 (n=271) |
| Oct-Nov 1975 (Baseline) | 24.1 | 40.9 | 63.2 | 40.0 | 48.1 | 38.8 |
| Apr-May 1976 | 22.2 | 27.1 | 47.4 | 30.0 | 43.4 | 21.1 |
| Oct-Nov 1976 | 11.1 | 13.1 | 29.7 | 30.8 | 17.6 | 31.0 |
| Apr-May 1977 | 6.3 | 13.1 | 16.7 | 12.3 | 7.0 | 12.8 |
| Oct-Nov 1977 | 11.8 | 18.2 | 22.8 | 13.4 | 13.8 | 12.5 |
| $Chi^2$ | 9.68 | 13.11 | 24.42 | 5.36 | 27.47 | 16.03 |
| P< | 0.05 | 0.025 | 0.001 | N.S. | 0.001 | 0.005 |

**Table 24. Changes in liver retinol, Guatemala, 1975-1977 (percent of samples by categories of retinol concentration).**

| Trimester period | No. | µg/g liver | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 0-50 | 51-100 | 101-150 | 151-200 | 201-250 | 251-300 | 301-350 | 351-400 | 401-450 | 451-500 | ≥ 500 |
| Oct-Dec 1975 | 79 | 25.3 | 22.8 | 21.5 | 8.9 | 6.3 | 7.6 | 3.8 | 1.3 | 0 | 0 | 2.5 |
| Jan-Mar 1976 | 67 | 28.4 | 20.9 | 17.9 | 9.0 | 11.9 | 3.0 | 6.0 | 1.5 | 1.5 | 0 | 0 |
| Apr-Jun 1976 | 111 | 15.3 | 21.6 | 23.4 | 17.1 | 8.1 | 4.5 | 4.5 | 0 | 1.8 | 0 | 3.6 |
| Jul-Sep 1976 | 151 | 8.6 | 11.9 | 17.2 | 18.5 | 13.9 | 10.6 | 4.0 | 2.6 | 4.6 | 2.6 | 5.3 |
| Oct-Dec 1976 | 111 | 6.3 | 21.6 | 17.1 | 16.2 | 12.6 | 9.0 | 5.4 | 3.6 | 0.9 | 2.7 | 4.5 |
| Jan-Mar 1977 | 123 | 11.4 | 17.9 | 20.3 | 13.8 | 13.0 | 6.5 | 5.7 | 4.1 | 2.4 | 1.6 | 3.3 |
| Apr-Sep 1977[1] | 123 | 2.4 | 8.1 | 21.1 | 15.4 | 23.8 | 11.4 | 2.4 | 4.1 | 1.6 | 3.3 | 7.3 |

[1]Semester

tion, which is partially supported by some liver reserves present at the end of pregnancy. By the fifth and sixth months the infant is still sucking strongly, because introduction of complementary artificial foods is not yet significant in these sociocultural settings. The fortification program, however, results in a very marked improvement, even at this time of lactation; it is evident that the effect of the additional intake of vitamin A by the woman through fortified sugar is to prevent this decrease in retinol breast milk content, as has been already emphasized by Arroyave et al. (*7*).

*Liver retinol.* This investigation, as mentioned previously, was conducted only in Guatemala City, and it is therefore indicative of the situation in the largest urban center in the country.

Table 24 gives the per cent distribution of liver retinol by categories of concentration in μg/g of tissue (50 μg ranges). The obvious and very significant effect ($Chi^2$ = 46.60; P < 0.001) is the decrease in the proportion of liver samples with 50 μg/g or less (see also Figure 10), and to a minor extent those with retinol concentrations between 51 and 100 μg/100 ml. Suthutvoravoot and Olson (*26*) have considered the breakpoint at 20 μg/g as more significant to characterize "deficient" reserves. The data illustrated in Figure 11 show that when this more critical criterion is applied, the decrease in "per cent of deficient" reserves (≤ 20 μg/g) from

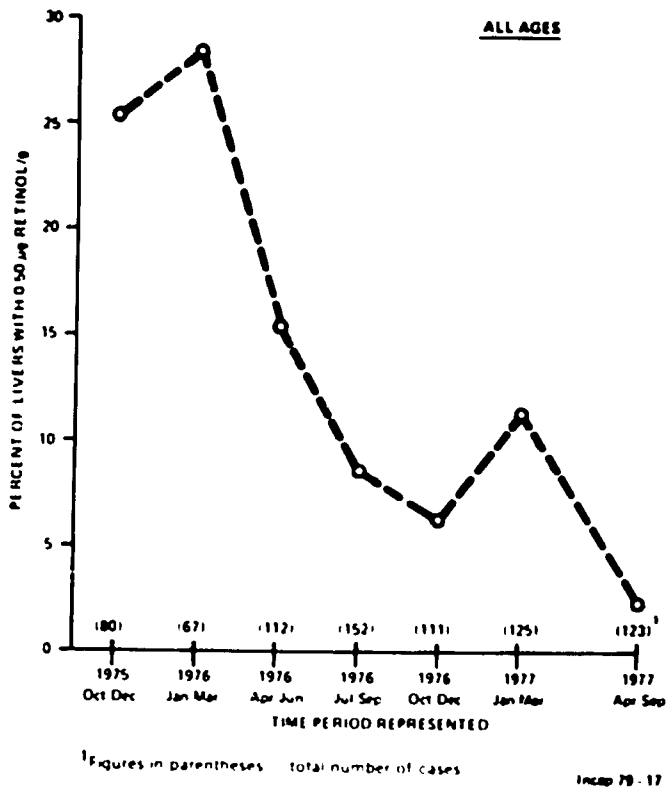


**Figure 10. Decrease in the percent of liver samples with retinol concentration of 50 μg per gram or less.**

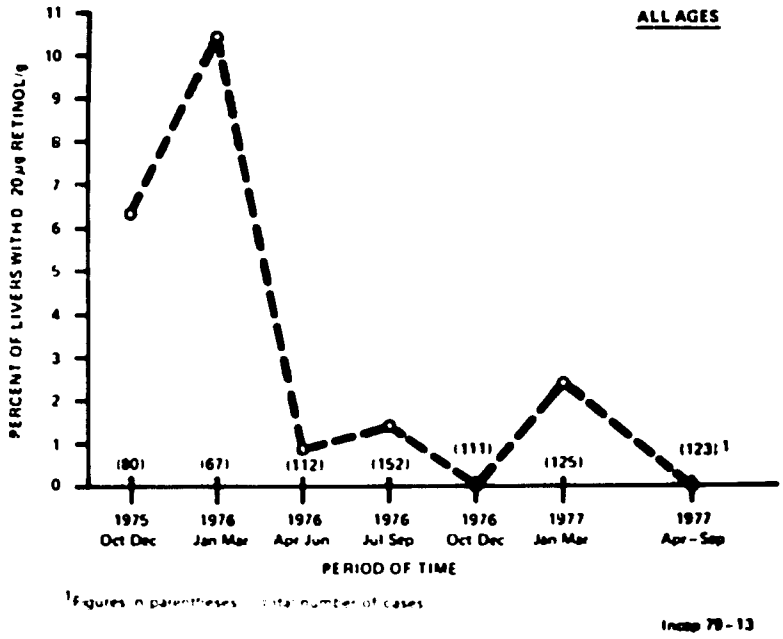


**Figure 11. Decrease in the percent of liver samples with retinol concentration of 20 µg per gram or less.**

October 1975 to September 1977 is just as dramatic and remains highly significant ($Chi^2$ = 36.82, P < 0.001). No specific explanation can be given for the "peaks" observed during the periods January-March in both 1976 and in 1977; since no dietary study was carried out in Guatemala City, one can only speculate that the peaks are due to the correspondence of these periods with the end of the dry season, when the availability of fresh green and yellow vegetable foods (carotene sources) is lowest for humans and of green pastures for dairy cattle. The graph in Figure 12 has been drawn from the data in Table 24 at the higher end of the spectrum of values. This curve illustrates that after a certain time the per cent of livers with concentrations of retinol in the higher levels did not tend to increase any further with the fortification. This information is important in that it indicates that the vitamin A in sugar at the fortification level used does not tend to result in increasing accumulation of liver retinol beyond a certain point.

Finally, percentile values for liver retinol are summarized in Table 25 confirming the increase in liver reserves observed through the two year evaluation period. The most relevant aspect of these data is that the lowest percentiles underwent the highest proportional improvement; for instance, the value of the 5th percentile increased nearly fivefold over the baseline figure and the 10th percentile more than threefold.

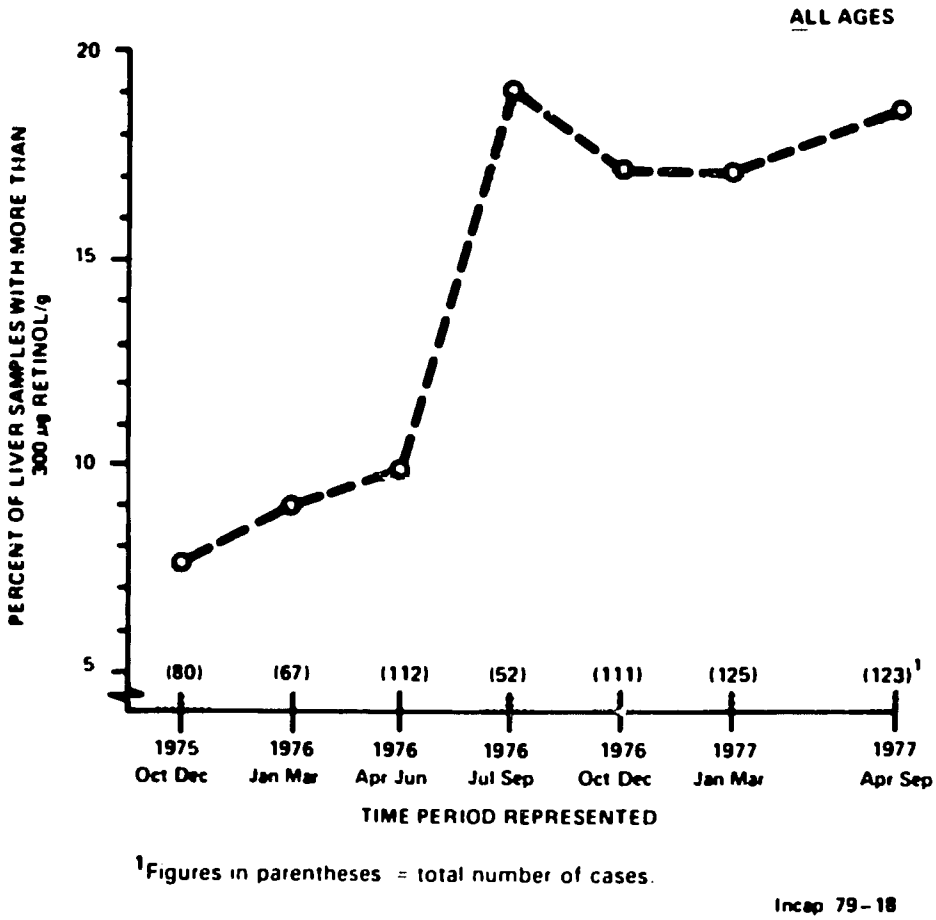


**Figure 12. Change in the percent of liver samples with more than 300 ug of retinol per gram.**

**Table 25. Changes in distribution of hepatic retinol concentration, Guatemala City, 1975-1977.**

| Trimester period | No. | Percentile values (µg/g liver tissue) | | | | |
|---|---|---|---|---|---|---|
| | | 5th | 10th | 50th | 90th | 95th |
| Oct-Dec 75 | 80 | 16 | 29 | 103 | 292 | 320 |
| Jan-Mar 76 | 67 | 15 | 20 | 103 | 256 | 313 |
| Apr-Jun 76 | 112 | 39 | 43 | 133 | 306 | 437 |
| Jul-Sep 76 | 152 | 30 | 53 | 175 | 420 | 568 |
| Oct-Nov 76 | 111 | 47 | 57 | 160 | 366 | 493 |
| Jan-Mar 77 | 125 | 40 | 46 | 157 | 380 | 493 |
| Apr-Sep 77[1] | 123 | 75 | 96 | 203 | 463 | 537 |

[1]Semester

## Ophthalmologic and Clinical Observations: Morbidity and Vitamin A Status

As has been already stated, the objective of the evaluation project was not to assess the clinical impact of the fortification, and its design is therefore not ideal to permit definitive conclusions in regard to morbidity changes. Nevertheless, since substantial numbers of children were examined during each survey, both for general morbidity and for ocular signs (conjunctival-corneal) attributable to vitamin A deficiency, it was found possible to carry out some analysis of the morbidity data and its association with vitamin A nutritional status.

Table 26 gives the individual findings of the ocular examination. Following the WHO classification (*19*), only conjunctival xerosis (X1A) and corneal scars (XS), were observed. The sign X1A was accepted for registration only when it was not doubtful. The following comments and observations seem of importance regarding these data:

a) The cases of corneal scars (XS) represent evidence of past events and therefore low serum levels are not necessarily expected to be associated with them at the moment of clinical examination; this is actually the case as seen in Table 26.

b) Cases of "active" lesions appeared only in the first two surveys. During the baseline survey (October-November 1975), there were two X1A cases out of 543 children, giving a ratio of 3.7/1,000. During the second survey (April-May 1976), only one case was seen out of 585 examined, with a ratio of 1.7/1,000. It is noteworthy that the serum retinol values for these three children were the lowest of all the cases with ocular involvement in all surveys, with the exception of the 54-month-old child in the first survey who only showed corneal scar in his left eye. It would be tempting to attribute the absence of "active" lesions during the last three surveys to the impact of the fortification program. This clinical information by itself would not even allow speculation in this respect, but if coupled with marked improvement in vitamin A dietary intake and biochemical nutritional status, it gains sufficient strength to support the suggestion of a cause-effect relationship. Observations of a long-term nature (several years) with an adequate design, will be necessary for confirmatory evidence.

c) All the cases where information could be obtained on general morbidity had suffered some disease of the type recognized as precipitating factors of xerophthalmia. This type of finding is not unique for the children with ocular lesions, but reflects instead the type of health environment of the rural families studied. It can only be hypothesized that eye lesions would not have developed in these children if they had not suffered the protein-energy malnutrition and the other morbidity encountered in them.

The association between general morbidity, especially infections, and decreased serum retinol levels has been widely recognized, and the cause-effect relationship was recently documented further by Arroyave and Calcaño (*22*). In order to investigate this relationship in the present study, the following analysis was carried out. Children with serum retinol levels in the "deficient" category (< 10 μg/100 ml) were selected at random and were matched for age and sex with children also selected at random from each of the following 10 μg-grouping: 10-19; 20-29; 30-39, and 40-49 μg/100 ml. Twenty-five age-sex matched pairs were obtained by the computer for each of the serum level categories.

The morbidity found in these children upon clinical examination is shown in Table 27. It is evident that the children with less than 10 μg of retinol per 100 ml have a significantly higher morbidity load, clearly distinguishing them from the others. Fever, respiratory disease, gastroenteritis, and edema are mostly responsible for the difference. The last column of Table 27 gives the proportion of children who showed two or more morbidity signs or disease entities. This indicator also separates the "deficient" serum retinol category as the most affected as evidenced by the significant difference found ($Chi^2 = 9.35$; $P < 0.025$). These data have additional intriguing epidemiologic appeal, since they indi-

**Table 26. Eye lesions attributable to vitamin A deficiency, Guatemala, 1975-1977.**

| Age (mo) | Retinol (µg/100 ml) | Conjunctival Xerosis (X1 A) | | Corneal Scars (XS) | | History and age[2] of onset lesion |
|---|---|---|---|---|---|---|
| | | r.e | l.e[1] | r.e | l.e | |
| Survey: Oct-Nov (Total group n = 543) | | | | | | |
| 18 | 19.11 | + | + | | | PEM[3] |
| 49 | 30.06 | | | | + | PEM |
| 54 | 15.38 | | | + | | PEM |
| 54 | 39.84 | | | | + | ---[4] |
| 57 | 40.54 | | | | + | --- |
| 58 | 3.50 | + | + | | | PEM |
| 65 | 39.84 | | | + | + | PEM |
| 69 | 24.47 | | | | + | --- |
| Survey: April-May 1976 (n = 585) | | | | | | |
| 20 | 11.47 | + | + | | | Systemic disease, diarrhea, PEM |
| 37 | 29.30 | | | | + | --- |
| 41 | 35.67 | | | | + | PEM, 30 mo. |
| 46 | 38.22 | | | | + | Measles, 12 mo. |
| Survey: Oct-Nov 1976 (n= 644) | | | | | | |
| 35 | 42.04 | | | | + | Fever (systemic disease?) 10 mo. |
| 48 | 40.77 | | | | + | Hospitalized for diarrhea and PEM, 12 mo. |
| 48 | 38.28 | | | | + | --- |
| 65 | 24.84 | | | + | + | Measles, 12 mo. |
| Survey: Apr-May 1977 (n = 676) | | | | | | |
| 21 | 31.28 | | | | + | Measles, 15 mo. |
| 27 | 43.01 | | | | + | --- |
| 40 | 35.97 | | | | + | PEM, 12 mo. |
| 48 | 26.59 | | | + | | Measles, 42 mo. |
| 60 | 23.46 | | | + | | Fever (systemic disease?) 59 mo. |
| 66 | 21.90 | | | | + | Fever (systemic disease?) 60 mo. |
| Survey: Oct-Nov 1977 (n = 721) | | | | | | |
| 47 | 39.10 | | | | + | Hospitalized for PEM, 24 mo. |
| 56 | 30.50 | | | | + | --- |
| 63 | 33.63 | | | | + | --- |

1) r.e= right eye; l.e= left eye; 2) when available; 3) Protein Energy Malnutrition; 4) no information

Table 27. Morbidity load in groups of children matched by age and sex and grouped in categories of serum retinol, Guatemala, 1975-1977.

| Retinol (µg/100 ml) | No. | Fever | Respiratory disease | Gastro-enteritis | Conjunc-tivitis | Conjunctival xerosis | Changes associated with PEM | | | Morbidity load[1] | Children with two or more morbidity signs or disease entities |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Hair | Lips | Edema | | |
| < 10 | 25 | 4 | 12 | 8 | 3 | 1 | 2 | 2 | 2 | 34/25 | 11/25 |
| 10-19 | 25 | 1 | 5 | 5 | 4 | - | 3 | - | - | 18/25 | 4/25 |
| 20-29 | 25 | - | 5 | 5 | 5 | - | 2 | 1 | | 18/25 | 4/25 |
| 30-39 | 25 | 2 | 9 | 2 | 3 | - | - | 1 | - | 17/25 | |
| 40-49 | 25 | 1 | 5 | 4 | 2 | - | | 1 | | 13/25 | 4/25 |

[1] Ratio between the total number of signs-symptoms and the total number of children

cate an important potential of serum retinol levels below 10 μg/100 ml as a public health indicator, at least in preschool children.

Another type of analysis combining the serum retinol data with the morbidity information is shown in Table 28. Here, the degree of morbidity is related to the serum retinol concentrations. During the analysis, it became apparent that for each subsequent survey over the two years, the number of children examined as "volunteers" (outside the preselected sample) increased. It was thought that the volunteer families might have attended the clinical examination center seeking medical attention to an ailment in any family member including their preschool children, biasing thereby the morbidity data. For this reason the analysis was done separately for the children in the preselected sample and those who attended as "volunteers."

The first thing to notice is that the number of "volunteer" children examined increased with each survey with a parallel increase in the cases with morbidity. The number of children in the preselected sample was essentially constant, and – although there was a trend in the number of cases with morbidity to increase – this was not nearly as marked and consistent as in the other subgroup.

The general features of these data relevant to the fortification program are: a) that the presence of morbidity results in a statistically significant decrease in serum retinol values ($P < 0.00001$) in any of the survey periods and in both groups; b) that the impact of three or more signs or symptoms in the children produces the most noticeable decreases in their serum retinol; c) that the increase in serum retinol with the fortification already described for the group at large, can also be observed both in the children with no disease and in those

**Table 28. Serum retinol concentration of preschool children according to the child's morbidity, Guatemala, 1975-1977 (μg/100 ml).**

| Survey period | Total No. | Number of clinical signs and symtoms registered in the child | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | none | | | one | | | two | | | three or more | | |
| | | n | $\bar{x}$ | S.D. | n | $\bar{x}$ | S.D | n | $\bar{x}$ | S.D. | n | $\bar{x}$ | S.D |
| | | | | | - Children in pre-selected sample- | | | | | | | | |
| Oct-Nov 75 | 195 | 246 | 31.2 | 9.7 | 101 | 26.6 | 10.6 | 34 | 26.6 | 12.2 | 14 | 22.8 | 8.6 |
| Apr-May 76 | 364 | 263 | 33.2 | 8.8 | 67 | 30.1 | 9.0 | 28 | 27.5 | 7.9 | 6 | 33.5 | 9.2 |
| Oct-Nov 76 | 375 | 141 | 36.2 | 9.6 | 142 | 34.1 | 9.9 | 61 | 36.0 | 8.3 | 31 | 30.6 | 7.3 |
| Apr-May 77 | 361 | 116 | 34.5 | 8.3 | 119 | 33.0 | 10.8 | 90 | 32.3 | 11.3 | 36 | 32.7 | 10.0 |
| Oct-Nov 77 | 322 | 104 | 32.4 | 10.2 | 137 | 32.5 | 9.2 | 65 | 31.8 | 8.8 | 16 | 25.3 | 6.4 |
| | | | | | -Other children- | | | | | | | | |
| Oct-Nov 75 | 146 | 88 | 29.7 | 11.8 | 43 | 25.7 | 9.5 | 11 | 27.4 | 12.3 | 4 | 15.1 | 8.7 |
| Apr-May 76 | 217 | 136 | 31.5 | 12.0 | 56 | 29.1 | 8.2 | 12 | 25.9 | 12.0 | 8 | 20.2 | 12.1 |
| Oct-Nov 76 | 266 | 76 | 34.2 | 8.6 | 106 | 34.3 | 8.0 | 64 | 33.5 | 8.4 | 20 | 34.2 | 10.7 |
| Apr-May 77 | 314 | 100 | 35.7 | 11.2 | 112 | 32.6 | 13.3 | 71 | 32.7 | 10.6 | 31 | 27.5 | 14.7 |
| Oct-Nov 77 | 394 | 112 | 31.7 | 8.6 | 164 | 31.9 | 8.2 | 82 | 30.8 | 8.8 | 36 | 26.8 | 9.6 |

with clinical signs or symptoms of disease, regardless of the child's morbidity load. This effect of the fortification was statistically highly significant ($P < 0.00001$); d) that the data analyzed in this manner point again to the observation, made in previous sections, that the impact of the fortification program on the biochemical parameters seems, as a whole, to have reached its highest point after the first year of fortification (October November 1976). In terms of the evaluation of the fortification it should be remarked, however, that even those children with heavier morbidity loads (2 and 3 or more) benefited by the higher intake of vitamin A resulting from the fortification

## Anthropometry: Growth and Vitamin A Status

As explained under "Methods," the body weights and heights of all the children were taken at the time of each clinical examination. One purpose of collecting these data was to obtain an indication of the general status of malnutrition of the groups of children, that is, what is generally referred to as protein energy malnutrition (PEM) but which, in effect, may be the consequence of multiple deficiencies including those of some vitamins and minerals. The main objective, however, of having these anthropometric indicators was to determine the relationship between the retinol serum levels of the children and their deficit in body weight and height. The analytical approach used for this purpose was similar to the one already applied in the case of morbidity. Children with serum retinol levels in the "deficient" category ($< 10 \mu g$ 100 ml) were selected at random and randomly matched for age and sex with children from each of the following 10 $\mu g$-groupings: 10-19; 20-29; 30-39, and 40-49 $\mu g$ 100 ml. Twenty-five age-sex matched pairs were obtained by the computer for each of the serum retinol level categories and the distribution of the subjects within each sub-group by weight age and weight height was found. Part A of Table 29 shows the results in relation to weight age. The $Chi^2$ test showed that as the serum retinol levels increase, the distribution of the children among the weight age categories improves significantly ($Chi^2 = 23.34$; $P < 0.025$). It was evident that the per cent of children with very large weight age deficit (< 60 per cent of standard), decreases notoriously as the serum retinol levels become higher, the group with less than 10 $\mu g$ 100 ml showing a distinguishing, higher proportion of cases with this magnitude of weight age deficit.

The analysis of the data in part B of Table 29 showed that when the critical indicator of present malnutrition (weight height) is applied there is also a significant relation between serum retinol and the distribution of the children among the weight height categories ($Chi^2 = 28.30$; $P < 0.005$). It is again evident in this case that the children with less than 10 $\mu g$ retinol per 100 ml are remarkably worse off than the rest. These data, together with those of the relationship between morbidity load and serum retinol levels, point to the epidemiologic significance of serum retinol levels less than 10 $\mu g$ 100 ml as indicators of health and nutrition risk.

In addition to the relationship just discussed, it was considered important to evaluate whether the beneficial effect of the fortification program on serum retinol levels already shown for the sample at large could also be detected in children regardless of their deficit in physical development, and to what extent. Table 30 shows data on the mean serum retinol levels of the children in relation to their weight height, weight age, and height age deficits, and the changes which were observed as the fortification was in effect through the two years of evaluation.

**Table 29. Distribution of weight deficit as a function of serum retinol levels in preschool children matched for age and sex, Guatemala, 1975–1977.**

PART A

| Serum retinol (µg/100 ml) | No. | Adequacy of weight/age (% of standard) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | <60 | | 60–74 | | 75–89 | | ≥ 90 | |
| | | n | % | n | % | n | % | n | % |
| < 10 | 25 | 7 | 28 | 12 | 48 | 4 | 16 | 2 | 8 |
| 10–19 | 25 | 3 | 12 | 7 | 28 | 10 | 40 | 5 | 20 |
| 20–29 | 25 | 4 | 16 | 4 | 16 | 11 | 44 | 6 | 24 |
| 30–39 | 25 | 2 | 8 | 9 | 36 | 12 | 48 | 2 | 8 |
| 40–49 | 25 | 0 | 0 | 6 | 24 | 16 | 64 | 3 | 12 |

PART B

| Serum retinol (µg/100 ml) | No. | Adequacy of weight/height (% of standard) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | < 80 | | 80–89 | | 90–99 | | ≥ 100 | |
| | | n | % | n | % | n | % | n | % |
| < 10 | 25 | 6 | 24 | 7 | 28 | 10 | 40 | 2 | 8 |
| 10–19 | 25 | 0 | 0 | 7 | 28 | 12 | 48 | 6 | 24 |
| 20–29 | 25 | 1 | 4 | 4 | 16 | 11 | 44 | 9 | 36 |
| 30–39 | 25 | 0 | 0 | 8 | 32 | 13 | 52 | 4 | 16 |
| 40–49 | 25 | 0 | 0 | 6 | 24 | 17 | 68 | 2 | 8 |

Part A of Table 30 presents the distribution of the children by weight height categories of adequacy for each of the survey periods, as well as the corresponding mean serum retinol values. By variance analysis it was shown that the serum retinol levels increase as the weight height improves ($P < 0.0025$). In addition, the effect of the fortification of sugar, as shown by the vertical comparison of the data, proved to be again highly significant ($P < 0.00001$).

In relation to weight age and height age two effects are notorious: a) the analysis of variance indicated that, independently of the specific survey-period, there was a highly significant trend for the serum retinol levels to become lower as the per cent deficit of standard weight or height became greater ($P < 0.0001$). Obviously the kind of data obtained through the present study design does not lend itself to concluding a cause effect relationship. It is tempting, however, to remark in this respect that one of the main manifestations of vitamin A deficiency in experimental animals is growth retardation and even growth arrest.

**Table 30. Relationship between serum retinol levels and weight and height deficits of the preschool children and changes associated with the fortification of sugar with vitamin A.**

PART A

| Survey period | Adequacy of weight/height (% of standard) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | < 80 | | | 80 - 89 | | | 90 - 99 | | | ≥ 100 | | |
| | n | $\bar{x}$ | S.D. | n | $\bar{x}$ | S.D. | n | $\bar{x}$ | S.D. | n | $\bar{x}$ | S.D. |
| Oct-Nov 75 | 22 | 22.5 | 13.4 | 162 | 29.7 | 10.7 | 234 | 29.3 | 11.0 | 110 | 27.6 | 9.8 |
| Apr-May 76 | 16 | 28.5 | 10.3 | 131 | 28.7 | 10.4 | 307 | 30.8 | 9.6 | 132 | 30.0 | 9.7 |
| Oct-Nov 76 | 11 | 38.1 | 8.6 | 127 | 33.8 | 8.6 | 334 | 34.7 | 8.6 | 167 | 34.6 | 10.1 |
| Apr-May 77 | 18 | 30.5 | 11.4 | 162 | 32.2 | 12.2 | 337 | 33.2 | 10.6 | 148 | 33.8 | 11.6 |
| Oct-Nov 77 | 12 | 24.0 | 11.5 | 154 | 31.8 | 9.7 | 370 | 31.8 | 9.5 | 177 | 31.5 | 8.6 |

PART B

| Survey period | Adequacy of weight/age (% of standard) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | < 60 | | | 60 - 74 | | | 75 - 89 | | | ≥ 90 | | |
| | n | $\bar{x}$ | S.D. | n | $\bar{x}$ | S.D. | n | $\bar{x}$ | S.D. | n | $\bar{x}$ | S.D. |
| Oct-Nov 75 | 28 | 24.4 | 12.7 | 201 | 28.3 | 11.2 | 240 | 29.6 | 10.3 | 60 | 29.6 | 10.1 |
| Apr-May 76 | 36 | 24.8 | 9.6 | 207 | 29.1 | 9.6 | 254 | 31.1 | 8.8 | 83 | 31.8 | 12.3 |
| Oct-Nov 76 | 11 | 30.5 | 12.0 | 221 | 34.1 | 8.5 | 304 | 34.8 | 9.0 | 104 | 35.4 | 10.0 |
| Apr-May 77 | 21 | 24.5 | 10.8 | 212 | 32.4 | 11.7 | 332 | 33.9 | 11.1 | 97 | 33.0 | 10.3 |
| Oct-Nov 77 | 29 | 27.6 | 14.4 | 249 | 31.1 | 8.6 | 337 | 31.6 | 9.6 | 81 | 34.1 | 8.6 |

PART C

| Survey period | Adequacy of height/age (% of standard) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | < 85 | | | 85 - 89 | | | 90 - 94 | | | ≥ 95 | | |
| | n | $\bar{x}$ | S.D. | n | $\bar{x}$ | S.D. | n | $\bar{x}$ | S.D. | n | $\bar{x}$ | S.D. |
| Oct-Nov 75 | 106 | 26.3 | 12.0 | 178 | 28.4 | 10.1 | 174 | 30.0 | 10.8 | 74 | 30.9 | 10.2 |
| Apr-May 76 | 143 | 28.0 | 9.2 | 183 | 30.3 | 9.1 | 170 | 30.6 | 9.9 | 84 | 32.2 | 11.5 |
| Oct-Nov 76 | 100 | 33.1 | 8.2 | 234 | 34.1 | 8.6 | 195 | 35.5 | 9.9 | 111 | 35.2 | 9.0 |
| Apr-May 77 | 107 | 31.0 | 11.8 | 216 | 34.0 | 11.8 | 212 | 32.5 | 10.2 | 126 | 33.8 | 11.5 |
| Oct-Nov 77 | 153 | 30.0 | 9.5 | 239 | 31.3 | 8.8 | 210 | 31.7 | 10.0 | 96 | 34.5 | 9.3 |

Nevertheless, the important implication remains that as the chronic anthropometric deficits become more severe the vitamin A nutritional status seems to worsen; b) from the point of view of the evaluation of the sugar fortification program, one can analyze these data in a vertical direction, that is, the changes in serum retinol associated with the improved retinol intake resulting from the program. Statistical analysis showed that for any of the categories of weight or height deficit there was a highly significant elevation of the mean serum levels from the baseline values (October November 1975) to the end of the evaluation (October November 1977) ($P < 0.0001$).

It may be noticed that regardless of the fact that the maximum improvement is evident in October November 1976 (first fortification year), it holds that even at the end of 1977 (second fortification year) the serum retinol values were still superior to those found before the fortification program and, in general, to a relatively similar extent for all subgroups of weight or height deficit. This indicates that the fortification reached even those nutritionally and probably socially least privileged children in the communities.

## Cost of the Fortification and Control

*Total cost per year.* Table 31 gives the estimated itemized and total cost per year, resulting from combining the information of the two years covered by the evaluation project. It is noteworthy that nearly 90 per cent of this total cost is due to the purchasing of the vitamin A product used. The price of this product (water dispersable retinol palmitate 250 CWS) per kg was US$11.00 for the first order (1975) and US$13.00 for the second order (1976). As determined by law, this cost was borne by the National Association of Sugar Manufacturers of Guatemala, as was that of the manufacturing of the premix carried out by INCAP.

*Cost per pound (lb) of fortified sugar.* Pounds (460 g) are used in Guatemala as the sugar retail weight unit. Throughout 1976-1977 the retail price was US$0.11/lb. Dividing the total cost of the program per year by the number of pounds of fortified sugar

**Table 31. Expense categories and total cost.**

| | Amount | Percent |
|---|---|---|
| Retinol Palmitate | US$ 395,432 | 89 |
| Manufacturing of premix | 42,000 | 9 |
| Transportation of premix | 3,500 | 1 |
| Monitoring: | | |
| Inspector (part-time) | 750 | |
| Chemical analysis | 500 | 1 |
| Inspector visits (transport) | 1,200 | |
| | $ 443,382 | 100 |

produced, it results in a fortification cost figure of US$0.0013 per pound, or US$0.13 per sack of 100 lb (qq = .46 kg). This represents only the 1.1 per cent of the retail price of sugar at the time.

*Cost per inhabitant per year.* Based on total population census figures (27) estimated for 1976, the cost of the fortification per person at the national level per year was US$0.07.

*Cost per "person protected."* In order to base these calculations on the best documented data, the following restricted criteria have been applied for the estimates: a) by "population protected" it is understood those children 1-5 years of age belonging to the *low* and *medium* income strata of the Guatemalan population at large (28), as shown in Table 32; b) "protection" is defined as the reduction in the number of low and medium income children in the categories of < 10 and < 20 μg 100 ml of serum retinol. The information presented in Table 33 was derived taking into consideration these criteria. A limitation of this approach could be that it is based on the premise that the population coverage of the intervention is 100 per cent, while the most realistic estimate is perhaps between 80 and 100 per cent (see section on estimates of the population coverage of the program). Being very critical, one could base the ratio "cost/protected child" on the lowest coverage, i.e., 80 per cent. The figures in the last column of Table 33 would then become US$20.02 and $3.66 for the < 10 and < 20 μg 100 ml criteria, respectively. On the other hand, it should be emphasized that the approach is very strict in view of the fact that it assumes that the preschool "children protected" were the only "persons protected" in the country. In reality, however, children outside of the 1-5-year-old range, pregnant and lactating women, and even other adults are also undoubtedly benefited.

It is proposed that, for an effort that has demonstrated to improve substantially the vitamin A intake and nutritional status of a population at large, the investment made seems unquestionably worthwhile.

## ESTIMATES OF THE POPULATION COVERAGE OF THE PROGRAM

Although the proportion of the population of the country potentially to be covered by the fortification of sugar with vitamin A was estimated before the implementation of the program, information obtained through its evaluation makes possible a rediscussion of this very relevant question. It is now documented that the sector of population

**Table 32. Estimated number of children by income strata.**[1]

| Stratum | Percent of total population | Per capita yearly income (US dollar) 1970 | Estimated 1-5 yrs old population |
|---|---|---|---|
| Low | 50 | 73 | 553,217 |
| Medium | 30 | 228 | 331,930 |
| Both | 80 | - | 885,147 |

[1]Reference (28)

**Table 33. Estimate of cost per child "protected."**

| Total number of children in low and medium income strata | With < 10 µg/100 ml | | | | Children "Protected" (I minus II) | Total cost per child "Protected" |
|---|---|---|---|---|---|---|
| | Before (I) | | After (II) | | | |
| | No. | (%) | No. | (%) | No. | (US$) |
| 885,147 | 29,210 | (3.3) | 2,655 | (0.3) | 26,555 | 16.69 |

| | With < 20 µg/100 ml | | | | Children "Protected" (I minus II) | Total cost per child "Protected" |
|---|---|---|---|---|---|---|
| | Before (I) | | After (II) | | | |
| | No. | (%) | No. | (%) | No. | (US$) |
| 885,147 | 190,306 | (21.5) | 45,142 | (5.1) | 145,164 | 3.05 |

represented by the main sample studied was covered by the delivery system. These "concentrated rural" people living in small communities in the range of 500-2,000 inhabitants represent around 1.5 million or 28 per cent of the total population.

There is no question that larger communities than the ones already discussed, having a higher level of urbanization and modernization in terms of basic services, a better general socioeconomic status, and a higher consumption of sugar (5) were more amply and intensively reached by the program, adding another two million (35 per cent) to the coverage.

The three independent additional delivery system studies described under "Methods," which were carried out in 17 ever smaller and less accessible rural villages (< 500 inhabitants), invariably showed that white sugar was available to them and being consumed by the families. In the 12 smallest rural villages (< 500 inhabitants) adjacent to the somewhat larger 12 communities of the main sample, it was found that 65 per cent of the households were consuming sugar with vitamin A, while in 35 per cent the white sugar sampled was not fortified, reflecting the incompleteness of the fortification at the factory level as already discussed. In the two other [illegible]ies (*Ie, II*) covering five remote villages between 69 and 200 inhabitants, a per capita daily consumption of white sugar ranging from 18 to 41 g was recorded. According to census figures the population living in this latter type of village amounts to 18 per cent of the total, resulting in a total estimate of 81 per cent coverage. To assume that the rest of the population (about 19 per cent) referred to by the Guatemalan Census Bureau as "rural dispersed" was not reached *at all* by the fortification program would result in an important underestimation, since the socioeconomic situation of this latter population group is known to be similar to the next higher stratum denominated "concentrated rural."

In conclusion, it may be reasonably estimated that through the fortification program, supplementary quantities of vitamin A reached the vast majority of the Guatemalan population.

## CONSIDERATIONS ON THE COMPARATIVE EFFICIENCY AND EFFECTIVENESS OF THE FORTIFICATION BETWEEN THE TWO YEARS OF EVALUATION

Table 17 already presented the average retinol intake per capita from natural food sources for each of the periods of study. It can be seen that through the two years of study there were only relatively small variations from survey to survey periods without any particular trend to either increase or decrease. These data are important because they serve as the basis for the conclusion that the improvement shown in the biochemical parameters of nutritional status with respect to vitamin A cannot be explained by a change in retinol intake from natural sources, but ought to be attributed to the contribution of the retinol in sugar. When retinol from sugar is added to retinol from natural sources figures are obtained for total retinol intake, which also appear in Table 17. The first thing to notice is the very significant improvement in the average per capita retinol intake over that from only natural sources. In general, as mentioned before, the intake of retinol equivalents tripled as a result of the fortification.

Although these data are valid for the program at large, they may be deceiving in terms of specific instances, as revealed when analyzed in more detail; the data as presented assume that all the sugar reaching the villages *all the time* was fortified at an estimated level of 10 μg of retinol per gram of sugar, as discussed elsewhere in this report. However, such data do not give

any indication of the "point-in-time" availability of fortified sugar through the two-year period, and evidence from other types of data suggests that this may have been less consistent during 1977. There are at least three documented instances when two large sugar factories did not fortify the sugar they were producing because of failure in the timely delivery of the premix. For 10-15 days these two factories produced white sugar without fortification which was equivalent to about 200,000 qq (46 kg-sacks). In addition, another factory produced 534,523 qq without vitamin A; this sugar was presumed to be destined only for certain industrial purposes legally exempted by law, but there is evidence that important amounts of the nonfortified sugar from this factory were channeled to direct table use. If this sugar without retinol had been randomly distributed among all the population, the impact of the fortification on the indicators of nutritional status for the sample studied would have been relatively insignificantly affected, since the total production of sugar was around four and a half million qq per year. However, there is a high probability that of the more than 700,000 unfortified sacks, shipments of appreciable size could have been delivered to some of the communities, resulting in relatively long periods of time when some of these communities may have been consuming sugar without vitamin A. This situation would be worse than if less concentrated fortified sugar would have been consumed continuously, providing the same total amount of retinol per year but without interruptions. This suggestion agrees with, and may explain, the biochemical data which indicate that the fortification during the season 1975-1976 as measured by the surveys carried out during 1976 had a stronger beneficial impact than the fortification during the season 1976-1977 as reflected by the surveys carried out during 1977.

This way of looking at the question is relevant for discussing the program with the persons and institutions responsible for performing the fortification and with those in charge of the control and supervision of the process, since it will make them realize the risk involved in not complying with the fortification in a regular and consistent manner. It is obvious that failure to fortify sugar for relatively long periods of time, especially in those factories which produce large quantities per day, will lead to a significant supply of sugar without vitamin A to certain sectors of the population (especially small communities), resulting in a less effective net dietary supplementation for those unfortunate cases. It is interesting that both the studies on breast milk retinol and the studies of serum retinol of preschool children suggest a less effective fortification during the 1976-1977 sugar production season. Although these conclusions are rather speculative, it was considered mandatory, as mentioned before, to draw attention to their significance, in order to assist all involved, particularly the producers and supervisors, in their efforts to improve the efficiency of fortification programs.

# Discussion

The Ten-Year Health Plan approved by the III Special Meeting of Ministers of Health of the countries of the Americas, and published by the Pan American Health Organization in January 1973 (*29*), contained, among others, the following two goals for the Member Governments: a) to reduce the present prevalence of hypovitaminosis A by 10 to 50 per cent (regional average 30 per cent)," and b) "to promote, where required, the approval of the necessary legislation to guarantee the fortifica- of selected basic foods with iron, vitamin A, vitamins of the B-complex, proteins and amino acids."

By that time the Institute of Nutrition of Central America and Panama (INCAP) had long since revealed through several studies the widespread occurrence of a serious deficit in dietary vitamin A among large majorities of the Central American people, particularly the rural and the socially deprived urban sectors (*1, 30*). The concern for this problem was deepened by the demonstration of a high prevalence of hypovitaminosis A among the same population groups, affecting particularly the young child. By self-mandate, INCAP started in 1969 research to discover the most feasible means to give a solution to this problem, research which led to the process of fortification of white table sugar with retinol palmitate. In 1971, the Ministers of Health of the countries of Central America and Panama, in their XVI Meeting in Panama City, resolved to: "Recommend to the respective Governments the fortification of sugar with vitamin A as a practical and effective method for correcting the prevailing vitamin A deficiency, and to urge them to take all measures necessary to overcome all economic, legal, and administrative difficulties that might occur in the application of the program in each one of the countries" (*31*).

This strong and clear mandate led INCAP to develop a new program of control of hypovitaminosis A in Central America and Panama. The story of the work carried out by this program in a multidisciplinary and multisectoral manner is long and complex, and the scope and nature of the present report do not allow it to be included with sufficient completeness and detail to do justice to the effort. Suffice it to repeat that sugar fortification with vitamin A is now being carried out by law at the national level in four countries of the Central American isthmus.

The work under discussion constitutes the report of the evaluation of the program in one of the countries, Guatemala, as a model with ample potential for generalization under similar ecologic, social, and political circumstances.

The central fact at this time is that, in terms of the dietary and biochemical features that define hypovitaminosis A, Guatemala is now significantly different and obviously better than before the sugar fortification program began. The goal set forth by the Ministers of Health of the Americas in relation to hypovitaminosis A has been amply achieved. The most vivid and, from the public health point of view, the most significant representation of this

positive change is depicted by the distribution curves of serum retinol of the preschool children, presented and discussed under "Biochemical Results." One ought not, however, to disregard the fact that other independently obtained data, such as breast milk retinol of rural lactating women and liver retinol in Guatemala City, point with paramount clarity towards the same outcome.

In conclusion, the program of fortification of sugar with vitamin A has definitely contributed to allow the population of this country to fulfill its individual and social right to an intake of vitamin A in accordance with that considered necessary for maintaining adequate nutrition with respect to this essential nutrient.

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# Appendices

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## APPENDIX 1

### Preparation of Vitamin A Premix for the Fortification of Sugar

*Basic Composition of the Vitamin A Premix*

| *Ingredient* | *1 kg* | *200 kg* |
|---|---|---|
| Vitamin A-250 CWS | 210.0 g | 42.0 kg |
| Peanut oil | 16.5 g | 3.3 kg |
| Stabilizer | 0.08 g | 16.5 g |
| Sugar | 773.42 g | 155.0 kg |

*Specifications of the Ingredients*

1. Retinol A palmitate-type 250 CWS from Hoffman-LaRoche. It should be certified with a potency of 250,000 IU per gram. (Other equivalent products authorized by INCAP can be used.)
2. Peanut oil-USP-free of peroxides. In addition to the usual specifications of the U.S. Pharmacopeia, this material should have a maximum peroxide content of 5 meq/kg. Peanut oil meeting these specifications can be obtained from: Mr. Pedro Montes de Oca, Goldkist International, P.O. Box 2210, Atlanta, Georgia 30301, USA.
3. Stabilizer mixture. The stabilizer is Ronoxan A from Hoffman-LaRoche (a note should be made of the date the material is received since it has an expiration date related to its effectiveness.)
4. White sugar (sucrose). This sugar must be dry and free-flowing.

*General Procedure for Preparation of the Premix*

*Preliminary Procedures*

The vitamin A powder and the sugar are premixed in an appropriate mixer. To this mixture, add the peanut oil containing the stabilizer and continue the mixing until uniformity is achieved. The finished premix is packed into double walled polyethylene bags, leaving a minimum of air space. The polyethylene bags are sealed and then packed into resistant paper bags.

*Manufacturing Procedures*

*Part A* Place 92 kg of sugar into an appropriate mixer. Next add 42 kg of vitamin A palmitate powder. Then add the balance of the sugar (63 kg) to complete the batch. Mix these ingredients until the blend appears uniform.

*Part B* Place 3.6 liters of peanut oil into a Pyrex glass container that can be fitted with a cover and a stirring device. Flush the container with nitrogen and leave an atmosphere of nitrogen over the oil. Add 16.5 g of the stabilizer mixture to the oil using constant agitation. Bubble nitrogen into the oil while mixing at 60°C in a constant temperature water bath. Continue the mixing until the stabilizer is dissolved (approximately 5 minutes at 60°C).

*Part C.* To the mixture of Part A slowly add the oily solution from Part B with constant mixing. After all of the oil has been added, continue mixing until the batch is uniform (approximately 10 minutes). Examine the final mixture visually to determine its uniformity.

### *Quality Control Specifications*

1. The premix should have a homogeneous pale yellow color and be in a free-flowing crystalline form.
2. The potency (activity) of the finished premix should be a minimum of 50,000 IU and a maximum of 55,000 IU per gram.

### *Comments and Precautions*

1. The low peroxide content of the peanut oil is critical. This required specification should be emphasized when the oil is ordered.
2. Once the can of Ronoxan A is opened it should be used as quickly as possible. It should be stored in a cold place to prevent deterioration.
3. The finished premix should not be exposed to direct sunlight or to conditions of high humidity.
4. The polyethylene packages should be completely filled leaving only a minimum of air space in the package.
5. The warehouse should be clean and dry with a temperature not to exceed 25°C. In areas where this is not possible the premix should be stored in the coolest place available.

## APPENDIX 2

The Government of Guatemala promulgated a decree, published on 28 June 1974 in the *Diario de Centro América*, stating that: "Sugar consumed in the country must be fortified with vitamin 'A,' in accordance with the standards established by the Ministry of Health and Social Welfare. . . ."


# Diario de Centro América

**ORGANO OFICIAL DE LA REPUBLICA DE GUATEMALA, C. A.**

**ANTES EL GUATEMALTECO**

Edificio de la Prensa Centroamericana
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Director Interino Periodista
Federico Zelaya Bochler
18 Calle 6-72, Zona 1

Fundado el 2 de Agosto de 1880
Teléfono de Administración 24-4-18

TOMO CIC — GUATEMALA, VIERNES 28 DE JUNIO DE 1974 — NUMERO 10


## DECRETO No. 58-74

**EL CONGRESO DE LA REPUBLICA DE GUATEMALA,**

CONSIDERANDO

Que diversos estudios realizados por organismos técnicos apropiados, han demostrado claramente que la población guatemalteca sufre de problemas nutricionales serios, uno de los cuales lo constituye el hecho de la marcada deficiencia de vitamina "A", responsable en alguna importancia de serias lesiones oculares y más de urgente entre los grupos vulnerables de menores recursos económicos.

CONSIDERANDO

Que es deber del Estado proteger la salud de los habitantes, dictando para el efecto las normas y medidas que tiendan a la defensa y mejoramiento de sus intereses, como lo es el de disponer el agregado del nutriente conocido como vitamina "A" a algunos de los alimentos de consumo general, a fin de superar su deficiencia en la dieta de los guatemaltecos de menores recursos económicos.

CONSIDERANDO:

Que se ha demostrado por estudios realizados por instituciones nacionales, regionales e internacionales de reconocida solvencia, que el azúcar refinada de consumo público es un vehículo adecuado para hacer llegar a todos los sectores de la población guatemalteca las cantidades mínimas de vitamina "A" indispensable para la protección contra la hipovitaminosis de este nutriente y para la conservación de la salud en general.

POR TANTO,

En uso de las facultades que le confiere el artículo 170, inciso 1o., de la Constitución de la República,

DECRETA:

Artículo 1o.—El azúcar centrifugada que se consuma en el país, deberá ser enriquecida con vitamina "A", de acuerdo con las normas que establezca el Ministerio de Salud Pública y Asistencia Social, en el reglamento respectivo.

Artículo 2o.—El Ministerio de Salud Pública y Asistencia Social supervisará el adecuado enriquecimiento del azúcar con vitamina "A", lo cual se hará bajo la responsabilidad de cada centro de producción o ingenio azucarero, en la forma que indique el reglamento.

Artículo 3o.—En tanto la vitamina "A" no se produzca en el país o en el área centroamericana, los representantes de los ingenios quedan autorizados para adquirirla en los mejores condiciones a nivel local o para importarla directamente, siempre que su calidad sea la adecuada y que su destino sea el que se refiere esta ley.

Artículo 4o.—Quedan libres de derechos arancelarios de importación, tasas, impuestos y demás contribuciones fiscales y municipales vigentes o que sean creadas en el futuro, la maquinaria, equipo, mercaderías, accesorios, repuestos y la vitamina "A", previa comprobación de que son necesarios para realizar el proceso de enriquecimiento del azúcar a que se refiere esta ley.

Artículo 5o.—Los costos del proceso de enriquecimiento y el valor del componente vitamínico serán absorbidos por el productor, sin que ello signifique para una alza en el precio del azúcar que se venda al consumidor final, salvo lo que establezca el reglamento.

Artículo 6o.—El sistema de enriquecimiento del azúcar con vitamina "A" deberá instalarse y entrar en funcionamiento, a partir de la zafra correspondiente al año 1974-75.

Artículo 7o.—El azúcar no enriquecida con vitamina "A" únicamente podrá dedicarse al mercado de exportación. Azúcar no enriquecida podrá dedicarse al mercado interno, con previa y expresa autorización del Ministerio de Salud Pública y Asistencia Social, y siempre que sea para aquellos casos en los que, en cada caso, se compruebe fehacientemente por un organismo técnico adecuado, la innecesariedad, la no justificación y o la incompatibilidad del aditivo.

Artículo 8o.—La comercialización de azúcar no enriquecida con vitamina "A" que se realice sin la autorización previa a que se refiere el artículo anterior, se considerará ilícita y se investigará a los responsables, los sancionados aplicables que establecen el Código de Salud.

Artículo 9o.—El Ejecutivo por conducto del Ministerio de Salud Pública y Asistencia Social, emitirá, en un plazo no mayor de noventa días a partir del día de la publicación de la presente ley en el Diario Oficial, un reglamento para la debida y oportuna aplicación de los preceptos contemplados en la misma.

Artículo 10.—Transitorio. Se exceptúan de la obligación de enriquecer el azúcar con vitamina "A" los existentes del producto elaborado que para el mercado interno que se hubieren producido en zafras anteriores a las que se determinan de conformidad con el artículo 6o. de la presente ley. Para el efecto, los interesados deberán informar oportunamente al Ministerio de Salud Pública y Asistencia Social al cuento de las existencias de dicho azúcar en esa fecha, para ejercer sobre las cantidades de dicho producto no enriquecido los controles que se estimen oportunos.

Artículo 11.—El presente Decreto entrará en vigor el día siguiente de su publicación en el Diario Oficial.

Pase al Organismo Ejecutivo para su publicación y cumplimiento.

Dado en el Palacio del Organismo Legislativo en la ciudad de Guatemala, a los nueve días del mes de junio de mil novecientos setenta y cuatro.

MARIO SANDOVAL ALARCON
Presidente.

MANFREDO HEMMERLING MORALES,
Secretario.

MARIATERESA F. DE GROTEWOLD
Secretaria.

Palacio Nacional: Guatemala, veintiocho de junio de mil novecientos setenta y cuatro.

Publíquese y cumplase.

CARLOS ARANA OSORIO

El Ministro de Salud Pública
y Asistencia Social,
JOSE TRINIDAD UCLES

## APPENDIX 3

### Rapid Colorimetric Method for the Control of the Fortification of Sugar with Vitamin A

A. *Description of the method*

1) Reagents

a) Chromogen reagent. To prepare this reagent weigh in a beaker 60 g of trichloroacetic acid and 40 g of methylene dichloride ($CH_2Cl_2$) or ethylene dichloride ($CH_2Cl{\cdot}CH_2Cl$). To dissolve completely, warm mixture in a water bath at 60-70°C with constant stirring. Store the reagent in an amber glass container with glass stopper.

b) Distilled water.

B. *Materials*

1) Test tubes 13 x 100 mm.
2) A measuring scoop (plastic or glass) which, when leveled, should contain approximately 500 mg (1/2 g) of sugar.
3) A small glass funnel to introduce the sugar into the test tube.
4) A dropper.
5) A 10 ml graduated syringe (glass or polyethylene) to measure the chromogen reagent. It is convenient to attach a length of polyethylene tubing to the tip of the syringe to facilitate delivery of the reagent into the test tube.
6) Color scale. In 13 x 100 mm test tubes place 4 ml of the following concentrations of copper sulfate water solution ($CuSO_4$, $5H_2O$) per 100 ml: 0.0, 1.0, 2.5, 5.0, 7.5, 10.0, 12.5, 20.0, and 25.0. Cover tubes with a rubber stopper sealing them airtight to prevent any evaporation. Label tubes from 1 to 9.

C. *Procedure*

With the measuring scoop place 500 mg of the sugar into a 13 x 100 mm test tube. Add 3 drops of distilled water and warm in a water bath at a temperature of 60-70°C for 1 minute; shake occasionally. Cool at room temperature in a cold water bath (± 20°C). Add with the measuring syringe 3 ml of the chromogen reagent and mix immediately. Compare against the color scale the blue color developed, which reaches its peak between 5-10 seconds. After 10 seconds the color begins to fade.

In our experience, using white sugar fortified within the limits recommended by the fortification program in Guatemala (43 to 57 IU per gram), the readings fall between tubes 6 and 9.

When the sugar being fortified is not completely white, but is instead yellow due to impurities, the color reaction tends to give a greenish color.

The colorimetric method permits rapid determination of whether a sample of sugar is or is not fortified with vitamin A, as well as the approximate level of fortification. For this reason it can be employed as a field method. For this purpose, the necessary reagents and materials can be placed in a portable box and transported directly to the places where one would wish to check the presence of vitamin A in the sugar.

## APPENDIX 4

### Some Ecologic and Socioeconomic Characteristics of the Communities

#### EL BARREAL

| | |
|---|---|
| *Location* | Jutiapa Department |
| *Distance from the capital of department* | 3 km by dirt road (117 km from Guatemala City) |
| *Altitude* | 905 meters above sea level |
| *Climate* | Dry temperate |
| *Population* | 1,123 inhabitants in 209 households |
| *Agriculture* | Corn, sorghum, cattle |
| *Industry* | Brick and clay artefacts |
| *Public services* | Primary school, electricity |
| *Drinking water* | Private wells |

#### SANTA MARIA IXHUATAN

| | |
|---|---|
| *Location* | Santa Rosa Department |
| *Distance from the capital city of Guatemala* | 81 km, last 15 km by dirt road in poor conditions |
| *Altitude* | 1,300 meters above sea level |
| *Climate* | Warm-wet |
| *Population* | 1,651 "ladinos" in 379 households |
| *Agriculture* | Corn, coffee |
| *Public services* | Primary school, health post, electricity, telegraph service |
| *Drinking water* | Domiciliary access |

#### SAN JUAN ZACAPA

| | |
|---|---|
| *Location* | Zacapa Department |
| *Distance from the capital of department* | 12 km by dirt road in good conditions (112 km from Guatemala City) |
| *Altitude* | 450 meters above sea level |
| *Climate* | Very warm-dry |
| *Population* | 1,233 "ladinos" in 267 households |
| *Agriculture* | Corn, sorghum, tomato, cattle |
| *Public services* | Primary school |
| *Drinking water* | Water comes from a nearby river and some public faucets |

#### EL JICARO

| | |
|---|---|
| *Location* | El Progreso Department |
| *Distance from Guatemala City* | 129 km, the last 12 km by dirt road in good conditions |
| *Altitude* | 242 meters above sea level |
| *Climate* | Very warm-dry |

| | |
|---|---|
| *Population* | 1,931 "ladinos" in 494 households |
| *Agriculture* | Corn, sorghum, tobacco |
| *Industry* | Palm-tree hats |
| *Public services* | Primary and high school, health center, social welfare center, electricity, telegraph |
| *Drinking water* | Domiciliary service |

BUENA VISTA

| | |
|---|---|
| *Location* | Quezaltenango Department |
| *Distance from Guatemala City* | 215 km |
| *Altitude* | 2,587 meters above sea level |
| *Climate* | Cold wet |
| *Population* | 1,139 mostly Indians of the "Mam" group in 253 households |
| *Agriculture* | Corn, wheat, favabeans, potatoes |
| *Industry* | Typical clothes |
| *Public services* | Primary school, private medical center |

SAN RAFAEL SACATEPEQUEZ

| | |
|---|---|
| *Location* | San Marcos Department |
| *Distance from Guatemala City* | 229 km, the last 2 km by dirt road in good conditions |
| *Altitude* | 2,700 meters above sea level |
| *Climate* | Cold-wet |
| *Population* | 1,123 predominantly Indians of the "Mam" group in 168 households |
| *Agriculture* | Corn, wheat, favabeans, potatoes |
| *Public services* | Primary school |
| *Drinking water* | Public pipettes |

SAQUITACAJ

| | |
|---|---|
| *Location* | Chimaltenango Department |
| *Distance from Guatemala City* | 112 km, the last 20 km by dirt road in poor conditions |
| *Altitude* | 2,100 meters above sea level |
| *Climate* | Cold-wet |
| *Population* | 771 Indians of the "Cakchiquel" group in 169 households |
| *Agriculture* | Corn, wheat, avocados, fruits |
| *Public services* | Primary school |
| *Drinking water* | The drinking water is a very deficient system |
| | During the earthquake of 1976 this village was seriously affected. |

LA LIBERTAD

| | |
|---|---|
| *Location* | San Marcos Department |
| *Distance from Guatemala City* | 336 km, the last 12 km by dirt road in good conditions |
| *Altitude* | 1,460 meters above sea level |
| *Climate* | Temperate wet |
| *Population* | 935, predominantly "ladinos," in 221 households |
| *Agriculture* | Corn, coffee |

| | |
|---|---|
| *Public services* | Primary school, health center, electricity, telegraph |
| *Drinking water* | Domiciliary access |

CUBULCO

| | |
|---|---|
| *Location* | Baja Verapaz Department |
| *Distance from Guatemala City* | 138 km, the last 40 km by dirt road in good conditions |
| *Altitude* | 1,200 meters above sea level |
| *Climate* | Dry-temperate |
| *Population* | 1,536 mixed "ladinos" and Indians of the "Quiché" group in 422 households |
| *Agriculture* | Corn |
| *Industry* | Commercial activities |
| *Public services* | Primary and high school, health center, electricity, telegraph |
| *Drinking water* | Domiciliary service |

SAN CARLOS ALZATATE

| | |
|---|---|
| *Location* | Jalapa Department |
| *Distance from Guatemala City* | 159 km, the last 21 km by dirt road in poor conditions |
| *Altitude* | 1,600 meters above sea level |
| *Climate* | Wet-temperate |
| *Population* | 1,327 predominantly "ladinos" in 286 households |
| *Agriculture* | Corn, wheat, coffee |
| *Public services* | Primary school, health center, telegraph |
| *Drinking water* | Deficient system of water service |

CAHABONCITO

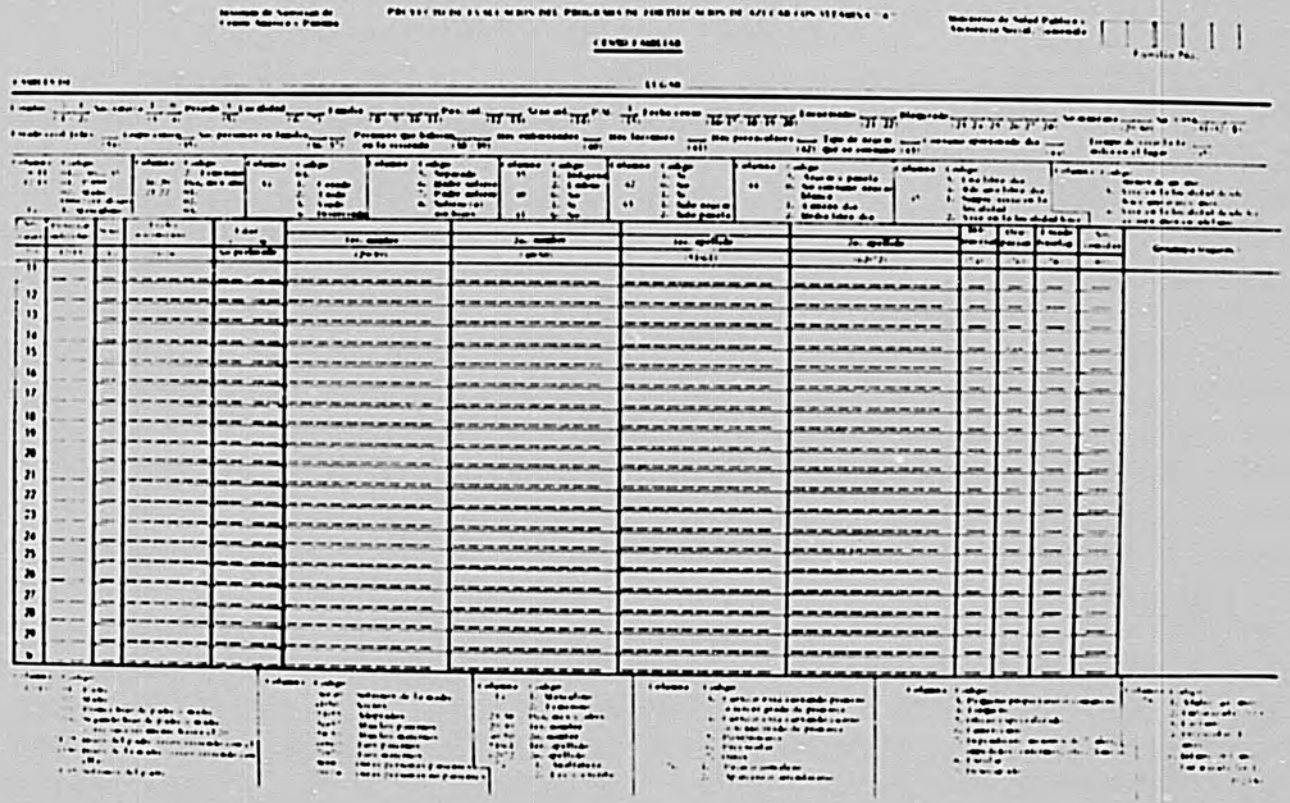
| | |
|---|---|
| *Location* | Alta Verapaz Department |
| *Distance from Guatemala City* | 320 km, 100 of which are dirt road |
| *Altitude* | 17 meters above sea level |
| *Climate* | Warm-wet |
| *Population* | 876 mostly Indians of the "Quekchi" group, in 205 households |
| *Agriculture* | Corn, rice |
| *Public services* | Primary school |
| *Drinking water* | It is obtained from a river or from little waterfalls |

SANTA FE

| | |
|---|---|
| *Location* | Retalhuleu Department |
| *Distance from Guatemala City* | 218 km |
| *Altitude* | 200 meters above sea level |
| *Climate* | Warm-wet |
| *Population* | 1,294 "ladinos" in 217 households |
| *Agriculture* | Corn, *ajonjolí*. Some inhabitants work for the nearby cotton plantations |
| *Public services* | Primary school, health post, no electricity |
| *Drinking water* | Pumpless wells |

## APPENDIX 5

In the pages that follow, examples are presented of the forms used to carry out the evaluation of the program of sugar fortification with vitamin A; they include the family census, a description of daily consumption of food, the details of the clinical examination of preschool children, and the test of hepatic retinol.



INSTITUTO DE NUTRICION DE CENTRO AMERICA Y PANAMA

INVESTIGACIONES DIETETICAS

CONSUMO DIARIO DE ALIMENTOS

PAIS: _____ LUGAR _____ ENCUESTADORA: _____

FAMILIA DE: _____ FECHA _____ DIA _____

(plato, clase, ingredientes, cantidades, pesos, precios, origen)

DESAYUNO

ausentes _____

visitas _____

ALMUERZO:

ausentes _____

visitas _____

ENTRE COMIDAS:

COMIDAS:

ausentes _____

visitas _____

RESTOS: _____ DESPERDICIOS: _____

PARA ANIMALES: _____ COMPRAS: _____

P-2331

**PROYECTO DE EVALUACION DEL PROGRAMA DE FORTIFICACION DE AZUCAR CON VITAMINA "A"**

Instituto de Nutrición de Centro América y Panamá

ENCUESTA DIETETICA

Ministerio de Salud Pública y Asistencia Social, Guatemala

**HOJA SUMARIO**

Nombre _____ Edad ____ ____ años meses

| Cols. | Estudio | Tarjeta |
|---|---|---|
| 1-4 | A 1 | 5 0 |

| Cols. | Período | Localidad |
|---|---|---|
| 5-7 | ___ | ___ ___ |

| Cols. | No. familia | Posición familiar |
|---|---|---|
| 8-16 | ___ ___ ___ ___ | ___ ___ |

| Sexo | Pertenece a la muestra |
|---|---|
| ___ | 1 |

| Cols. | Fecha encuesta | Encuestador |
|---|---|---|
| 18-22 | ___ ___ ___ ___ ___ | ___ ___ |

| Cols. | Asistencia | Método |
|---|---|---|
| 23-27 | ___ ___ ___ ___ | ___ |

| Número alimento (28-30) | ALIMENTO | Desayuno | Almuerzo | Entre comidas | Cena | Total peso bruto | Peso neto % | Total peso en gramos (31-36) |
|---|---|---|---|---|---|---|---|---|
| ___ | | | | | | | | ___ ___ ___ ___ |
| ___ | | | | | | | | ___ ___ ___ ___ |
| ___ | | | | | | | | ___ ___ ___ ___ |
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| ___ | | | | | | | | ___ ___ ___ ___ |
| ___ | | | | | | | | ___ ___ ___ ___ |
| ___ | | | | | | | | ___ ___ ___ ___ |
| ___ | | | | | | | | ___ ___ ___ ___ |

P. 2000

PROYECTO DE EVALUACION DEL PROGRAMA DE FORTIFICACION
DE AZUCAR CON VITAMINA "A"

Instituto de Nutrición de
Centro América y Panamá

Ministerio de Salud Pública y
Asistencia Social, Guatemala

EXAMEN CLINICO EN NIÑOS PREESCOLARES

Nombre _____ Edad ____ ____

| Cols. | Estudio | Tarjeta |
|---|---|---|
| 1-4 | A 1 | 0 6 |

| Cols. | Período | Localidad |
|---|---|---|
| 5-7 | 1 | ___ ___ |

| Cols. | No. familia | Posición familiar | Sexo | Pertenece a la muestra |
|---|---|---|---|---|
| 8-15 | ___ ___ ___ ___ | ___ ___ | ___ | ___ |

| Cols. | Fecha encuesta | Encuestador |
|---|---|---|
| 16-22 | ___ ___ ___ ___ ___ | ___ ___ |

| Cols. | Fecha nacimiento |
|---|---|
| 23-29 | ___ ___ ___ ___ ___ ___ |

| Cols. | Peso lbs. | onzas |
|---|---|---|
| 29-32 | ___ ___ | ___ ___ |

| Cols. | Talla cms. |
|---|---|
| 33-36 | ___ ___ ___ ___ |

| Cols. | Hospital |
|---|---|
| 37-38 | ___ ___ |

Enfermedades (39-80)

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 01 | | ENFERMEDADES INFECTO CONTAGIOSAS | | 04 | 06 | Neumonía, pulmonía, bronconeumonía | |
| 01 | 01 | Sarampión | | 04 | 07 | Infección respiratoria superior | |
| 01 | 02 | Varicela | | 04 | 08 | Laringitis, ronquera, afonía | |
| 01 | 03 | Eruptivo no identificado | | 04 | 09 | Amigdalitis | |
| 01 | 04 | Tos ferina | | 04 | 10 | Asma | |
| 01 | 05 | Paperas, parotiditis | | 04 | 11 | Sangre de nariz | |
| 01 | 06 | Gripe, influenza, catarro febril | | 04 | 12 | Otras | |
| 01 | 07 | Otras | | 05 | | ENFERMEDADES DIGESTIVAS | |
| 02 | | SINTOMAS GENERALES | | 05 | 01 | Diarrea (lactantes) inf. intestinal, enterocolitis | |
| 02 | 01 | Calentura, fiebre | | 05 | 02 | Disentería (lactantes con sangre) amebiasis | |
| 02 | 02 | Escalofríos, sudor frío | | 05 | 03 | Vómitos, nausea | |
| 02 | 03 | Cefalea, cefalea frontal, jaqueca, dolor de cabeza, dolor cerebral | | 05 | 04 | Parásitos, parasitismo intestinal | |
| | | | | 05 | 05 | Otras | |
| 02 | 04 | Palidez | | 06 | | ORGANOS DE LOS SENTIDOS | |
| 02 | 05 | Debilidad, falta de fuerza, decaimiento, hipotonía muscular | | 06 | 01 | Conjuntivitis | |
| | | | | 06 | 02 | Escupela (orzuelos) | |
| 02 | 06 | Edema, hinchazón generalizada | | 06 | 03 | Dolor de oídos | |
| 02 | 07 | Hinchazón de piernas | | 06 | 04 | Otitis purulenta | |
| 02 | 08 | Adelgazamiento | | 06 | 05 | Otras | |
| 02 | 09 | Pérdida de apetito, anorexia | | | | EXAMEN FISICO: SIGNOS DE D.P.C. | |
| 02 | 10 | Deshidratación | | 07 | | PELO | |
| 03 | | ENFERMEDADES DE LA PIEL | | 07 | 01 | Pelo fino | |
| 03 | 01 | Manchas | | 07 | 02 | Seco | |
| 03 | 02 | Granos, ronchas | | 07 | 03 | Despigmentado | |
| 03 | 03 | Abscesos, furúnculos | | 07 | 04 | Fácilmente desprendible | |
| 03 | 04 | Infecciones purulentas, celulitis | | 07 | 05 | Signo de bandera | |
| 03 | 05 | Ulceraciones | | 08 | | PIEL | |
| 03 | 06 | Picazón en el cuerpo, picazón en la cara y cuello | | 08 | 01 | Hiperqueratosis folicular en la espalda | |
| | | | | 08 | 02 | Hiperqueratosis folicular en los brazos | |
| 03 | 07 | Infecciones piel, dermatitis, sarcoptosis | | 08 | 03 | Pigmentación | |
| 03 | 08 | Caída del cabello | | 08 | 04 | Descamación | |
| 03 | 09 | Otras | | 09 | | LABIOS | |
| 04 | | ENFERMEDADES RESPIRATORIAS | | 09 | 01 | Fisuras en los ángulos de los labios | |
| 04 | 01 | Tos | | 09 | 02 | Cicatrices angulares | |
| 04 | 02 | Catarro | | 09 | 03 | Queilosis | |
| 04 | 03 | Hervor de pecho | | 10 | | EDEMA | |
| 04 | 04 | Fatiga | | 10 | 01 | Pretibial | |
| 04 | 05 | Bronquitis | | 10 | 02 | Generalizado | |

Observaciones:

P-2316d

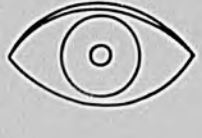
ENCUESTA OFTALMOLOGICA

| EXAMEN OCULAR | Ojo derecho | | | Ojo izquierdo | | |
|---|---|---|---|---|---|---|
| 11 PARPADOS | | | | | | |
| Edema palpebral | 11 | 01 | | 11 | 51 | |
| Blefaritis marginal | 11 | 02 | | 11 | 52 | |
| Orzuelos | 11 | 03 | | 11 | 53 | |
| Chalazión | 11 | 04 | | 11 | 54 | |
| 12 CONJUNTIVA | | | | | | |
| Mancha de Bitot | 12 | 01 | | 12 | 51 | |
| Depósitos en superficie | 12 | 02 | | 12 | 52 | |
| Xerosis discreta | 12 | 03 | | 12 | 53 | |
| Xerosis moderada | 12 | 04 | | 12 | 54 | |
| Xerosis marcada | 12 | 05 | | 12 | 55 | |
| Pigmentación gris bulbar | 12 | 06 | | 12 | 56 | |
| Pigmentación gris fondo de saco | 12 | 07 | | 12 | 57 | |
| Pigmentación gris tarsal | 12 | 08 | | 12 | 58 | |
| Pigmentación negra bulbar | 12 | 09 | | 12 | 59 | |
| Pigmentación negra fondo de saco | 12 | 10 | | 12 | 60 | |
| Pigmentación negra tarsal | 12 | 11 | | 12 | 61 | |
| 13 CORNEA | | | | | | |
| Xerosis discreta | 13 | 01 | | 13 | 51 | |
| Xerosis moderada | 13 | 02 | | 13 | 52 | |
| Xerosis marcada | 13 | 03 | | 13 | 53 | |
| Depósitos en superficie | 13 | 04 | | 13 | 54 | |
| Enturbamiento del estroma corneal | 13 | 05 | | 13 | 55 | |
| Enturbamiento del estroma corneal con hipema | 13 | 06 | | 13 | 56 | |
| Enturbamiento del estroma corneal con exudado en cámara anterior | 13 | 07 | | 13 | 57 | |
| ULCERA CORNEAL | | | | | | |
| Ulcera corneal central | 13 | 08 | | 13 | 58 | |
| Ulcera corneal periférica | 13 | 09 | | 13 | 59 | |
| Ulcera corneal superior | 13 | 10 | | 13 | 60 | |
| Ulcera corneal inferior | 13 | 11 | | 13 | 61 | |
| Ulcera corneal nasal | 13 | 12 | | 13 | 62 | |
| Ulcera corneal temporal | 13 | 13 | | 13 | 63 | |
| Ulcera corneal parcial | 13 | 14 | | 13 | 64 | |
| Ulcera corneal total | 13 | 15 | | 13 | 65 | |
| | | | | | | |

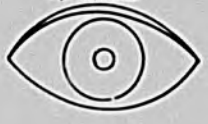
| EXAMEN OCULAR | Ojo derecho | | | Ojo izquierdo | | |
|---|---|---|---|---|---|---|
| 14 QUERATOMALACIA | | | | | | |
| Parcial | 14 | 01 | | 14 | 51 | |
| Total | 14 | 02 | | 14 | 52 | |
| Con estafiloma | 14 | 03 | | 14 | 53 | |
| Con engrosamiento y emblanquecimiento de la cornea | 14 | 04 | | 14 | 54 | |
| Descemetocele | 14 | 05 | | 14 | 55 | |
| Perforación corneal | 14 | 06 | | 14 | 56 | |
| Prolapso de iris | 14 | 07 | | 14 | 57 | |
| SECUELAS | | | | | | |
| 15 LEUCOMA | | | | | | |
| Leucoma central | 15 | 01 | | 15 | 51 | |
| Leucoma periférico | 15 | 02 | | 15 | 52 | |
| Leucoma superior | 15 | 03 | | 15 | 53 | |
| Leucoma inferior | 15 | 04 | | 15 | 54 | |
| Leucoma nasal | 15 | 05 | | 15 | 55 | |
| Leucoma temporal | 15 | 06 | | 15 | 56 | |
| Leucoma parcial | 15 | 07 | | 15 | 57 | |
| Leucoma total | 15 | 08 | | 15 | 58 | |
| Leucoma blanquecino | 15 | 09 | | 15 | 59 | |
| Leucoma vascularizado | 15 | 10 | | 15 | 60 | |
| Leucoma adherente | 15 | 11 | | 15 | 61 | |
| 16 ESTFILOMA CORNEAL | 16 | 01 | | 16 | 51 | |
| 17 ATROFIA DEL GLOBO OCULAR (Phthisis bulbi) | 17 | 01 | | 17 | 51 | |
| 18 GLAUCOMA SECUNDARIO | 18 | 01 | | 18 | 51 | |
| 19 AGUDEZA VISUAL | | | | | | |
| 20/20 - 20/200 | 19 | 01 | | 19 | 51 | |
| 20/200 - 20/400 | 19 | 02 | | 19 | 52 | |
| Cuenta dedos, movimiento de manos | 19 | 03 | | 19 | 53 | |
| Percepción de luz | 19 | 04 | | 19 | 54 | |
| Se desplaza sin dificultad | 19 | 05 | | 19 | 55 | |
| Se desplaza con dificultad | 19 | 06 | | 19 | 56 | |
| Necesita ayuda para desplazarse | 19 | 07 | | 19 | 57 | |
| 20 DIAGNOSTICO | | | | | | |
| Grado de lesión ocular | | | | | | |
| Enfermedad concurrente | | | | | | |
| 21 SOBREVIVENCIA | | | | | | |

Observaciones: _____

Ojo derecho



Ojo izquierdo



P-2316 d

LAB

PROYECTO DE EVALUACION DEL PROGRAMA DE FORTIFICACION DE AZUCAR CON VITAMINA "A"

Instituto de Nutrición de Centro América y Panamá

Ministerio de Salud Pública y Asistencia Social, Guatemala

Servicio Médico Forense
Adscrito al Organismo Judicial
Departamento de Patología
Hospital General

ESTUDIO DE RETINOL HEPATICO

Nombre _____ Edad ___ ___
años meses

| Cols. | Estudio | Tarjeta |
|---|---|---|
| 1-4 | A 1 | 0 1 |

| Cols. | Período | Localidad |
|---|---|---|
| 5-7 | 1 | ___ ___ |

| Cols. | Bloqueado | Cols. | Sexo | Pertenece a la muestra |
|---|---|---|---|---|
| 8-13 | | 14-15 | ___ | 0 |

| Cols. | Fecha de la autopsia | | | Encuestador |
|---|---|---|---|---|
| 16-22 | ___ ___ día | ___ ___ mes | ___ año | ___ ___ |

| Cols. | Fecha nacimiento | | |
|---|---|---|---|
| 23-28 | ___ ___ día | ___ ___ mes | ___ ___ año |

| Cols. | Peso | Talla |
|---|---|---|
| 29-35 | ___ ___ ___ kg | ___ ___ ___ cms |

| Cols. | Peso hígado |
|---|---|
| 36-39 | ___ ___ ___ ___ gr |

| Cols. | Diagnóstico macroscópico del hígado |
|---|---|
| 40 | ___ |

| Cols. | Diagnóstico microscópico del hígado |
|---|---|
| 41 | ___ |

| Cols. | Hora de la muestra | |
|---|---|---|
| 42-45 | ___ ___ horas | ___ ___ minutos |

| Cols. | Hora de la autopsia | |
|---|---|---|
| 46-49 | ___ ___ horas | ___ ___ minutos |

| Cols. | Causa de la muerte |
|---|---|
| 50-52 | ___ ___ ___ |

| Cols. | Número de la autopsia | Hospital |
|---|---|---|
| 53-58 | ___ ___ ___ ___ | ___ ___ |

Exclusivo para uso del Laboratorio

| Cols. | Retinol | Clave Laboratorio |
|---|---|---|
| 59-68 | ___ ___ ___ ___ | ___ ___ ___ ___ ___ ___ |

Originario de: _____

Observaciones: _____

F-2316 e

## APPENDIX 6

### Personnel Who Participated in the Evaluation of Sugar Fortification with Vitamin A at the National Level

**Guatemala, 1975-1977**

*Professional staff*

| | |
|---|---|
| Guillermo A[illegible]oyave, Ph.D. | Program director |
| Juan Rod[illegible] Aguilar, M.D., M.P.H. | Field director |
| Marina F[illegible]s, M.Sc. | Chief, Dietary Research Section, Division of Applied Nutrition |
| Miguel A. Guzmán, Ph.D. | Chief, Division of Statistics |
| Ivan D. Beghin, M.D., M.Sc. | Chief, Division of Applied Nutrition |
| Simón Sibony | Programmer, Computer Center |
| Beatriz Pellecer | Chief secretary |

*Consultants*

| | |
|---|---|
| Dr. Humberto Escapini | Chief, Ophthalmology Department, Bloom Hospital, San Salvador, El Salvador |
| Dr. Jules J. M. Sauter | Lecturer in Ophthalmology, Muhimbili Medical Center, Dar es Salaam, Tanzania |
| Mr. Eusebio G. Portela | Chief engineer, Ingenio El Salto, Escuintla, Guatemala |

*Field personnel* (not necessarily working simultaneously)

| | |
|---|---|
| Ana María Aguilar | Field worker |
| María Aguilar Sosa | Field worker |
| Norma Aracely Roldán | Field worker |
| Vilma Ortiz Monroy | Field worker |
| Eva Adalina Zabala | Field worker |
| Mirna Ruth Coronado | Field worker |
| Idalma Mazariegos | Field worker |
| María Antonieta Ramírez | Field worker |
| Ulda de Aguilar | Anthropometrist |
| María Isabel de la Cruz | Dietary supervisor |
| Zoila Flores | Dietary supervisor |
| Teresita de J. Miranda | Laboratory assistant |
| César Reyes | Laboratory assistant |
| Marina de Aldana | Laboratory technician |
| Carlotha de Funes | Laboratory technician |
| Ana Patricia Funes | Laboratory assistant |
| José Antonio Lanuza | Pilot |
| Virgilio López González | Pilot |

| | |
|---|---|
| Marco Tulio de León | Pilot |
| Guillermo Rodas | Pilot |
| Héctor Eduardo Flores | Data clerk |
| Otto Moratava | Data clerk |
| Jerjes Argueta | Data clerk |
| Anselmo Alvarez | Data clerk |
| Vinicio Ocaña | Data clerk |
| Rosa Elena Rivadeneira | Secretary |
| Laura María Jiménez | Secretary |
| Leopoldo Bolaños Bendfeldt | Field physician |
| Silvia Franzetti | Field physician |
| Silvia Castañeda | Field physician |
| Héctor Lucero | Field physician |
| Antonio Matute Morales | Field physician |
| Guillermo Tello | Physician |

*Other personnel* (Tutorial Training Fellows)

Patricia La Rue
Margaret Goetz

## APPENDIX 7

### Dissemination and Utilization of Research Results

During the period covered by this report, the investigators have devoted a significant amount of time and effort to present to the public at various levels the bases, objectives, and accomplishments of the program. Emphasis has been given to the importance that this evaluation scheme has in order to determine the value of the intervention. The different audiences have included technicians in the health and sugar manufacturing sector, medical and paramedical personnel, government officials and scientists in the food and nutrition field, as can be seen in the list of examples included in this appendix.

In the performance of the work, especially in the field operation, local personnel have taken part as members of such technical teams as dietary, clinical, anthropometric, and biochemical teams. In El Salvador for example, twelve such technical people were involved including a physician and three nutritionists. In Guatemala, in addition to the indispensable input—including financial assistance—of the National Association of Sugar Manufacturers in the management of the fortification, research on the assessment of the delivery system directly involved a supervisor-engineer from the Association's staff as well as the chief engineers of all the sugar mills.

A special manual has been prepared and published in order to assist in the continuous evaluation, supervision, and control of the fortification process and the delivery system.

Nearly 500 slides have been prepared both in English and Spanish, illustrating phases of the field survey work and other different aspects of the program, including evaluation data.

## APPENDIX 8

### Scientific Work, Seminars, Conferences, and Lectures related to the Evaluation of the Fortification of Sugar with Vitamin A.

*Theses and monographs*

Franzetti, S. E. Efecto de la morbilidad sobre los valores de retinol séricos encontrados en preescolares. Medical Sciences Faculty, University of San Carlos of Guatemala/INCAP, 1976.

Ruiz, T. Estudio de hipovitaminosis A en el Nor-Este brasileiro y la fortificación de azúcar blanca como medida probable para la solución del problema. Medical Sciences Faculty, University of San Carlos of Guatemala/INCAP, 1975.

Matute Morales, A. Niveles de hemoglobina en la población rural de Guatemala de 12 a 72 meses—estudio preliminar para la correlación de anemias ferropriva y deficiencia de vitamina A. Medical Sciences Faculty, University of San Carlos of Guatemala/INCAP, 1977.

Zarate Zarate, A. R. Evaluación del consumo de azúcar fortificada con vitamina A en tres comunidades rurales de la República de Guatemala. School of Chemical Sciences and Pharmacy, University of San Carlos of Guatemala/INCAP/CESNA School of Nutrition, 1978.

*Manuals*

Manual de Operaciones para la Fortificación de Azúcar con Vitamina A. INCAP, 1975.

Manual de Supervisión y Control de Programas de Fortificación de Azúcar con Vitamina A. INCAP, 1977.

*Publications and Congressional Presentations*

Aguilar, J. R., G. Arroyave, and E. Portela. Rapid method for adding vitamin A to sugar at an industrial level. Proceedings of the X International Congress of Nutrition (Kyoto, Japan, 3-9 August 1975). Abstract, Symposia and Free Communications, pp. 339.

Arroyave, G., J. C. Bauernfeind, J. A. Olson, and B. A. Underwood. Selection of intervention strategies. IVACG Task Force on Intervention. In: *Guidelines for the Eradication of Vitamin A Deficiency and Xerophthalmia—A Report of the International Vitamin A Deficiency Group-IVACG* (Meeting held in Port-au-Prince, Haiti, 23-25 March 1976). New York, Nutrition Foundation, Inc., 1976, pp. II-1-8.

Pettis, S. T., G. Arroyave, B. A. Underwood, et al. Evaluation of selected vitamin A intervention strategies. In: *Guidelines for the Eradication of Vitamin A Deficiency and Xerophthalmia—A Report of the International Vitamin A Consultative Group-IVACG* (Meeting held in Port-au-Prince, Haiti, 23-25 March 1976). New York, Nutrition Foundation, Inc., 1976, pp. III-1-10.

Arroyave, G. Evaluation of sugar fortification with vitamin A at the national level.

Paper given at the Conference at the National Eye Institute – Workshop on Keratomalacia (Bethesda, Maryland, 28-29 October 1976).

Arroyave, G. Modes of intervention and difficulties in their implementation in Central America. Conference for the Nutrition Intervention Feasibility in Developing Countries (organized by Hoffmann-LaRoche, Inc., Nutley, New Jersey, 25 October 1976).

Aguilar, J. R., G. Arroyave, M. Flores, S. Sibony, and I. Beghin. Evaluación de la efectividad biológica del programa de fortificación de azúcar con vitamina A (PROVITA) en Guatemala – Metodología y resultados preliminares. IV Latin American Congress on Nutrition (Caracas, Venezuela, 21-27 November 1976).

Flores, M., G. Arroyave, J. R. Aguilar, and I. Beghin. Niveles y origen de la vitamina A en las dietas de poblaciones rurales de Guatemala. IV Latin American Congress on Nutrition (Caracas, Venezuela, 21-27 November 1976).

Arroyave, G. Dietary deficit of vitamin A in populations – Approaches to correct it. Annual Meeting of the Food and Nutrition Liaison Committee. The Nutrition Foundation, Inc. (24-27 January 1978, Naples, Florida).

Arroyave, G., J. R. Aguilar, and M. Flores. Evaluation of programs to control vitamin A deficiency. V Western Hemisphere Nutrition Congress (Quebec, Canada, 15-18 August 1977). In press.

Portela, E., G. Arroyave, and J. R. Aguilar. Improving sugar for better nutrition – Fortification with vitamin A at national level. In Reis, F. S., and J. Dick (eds.), *Factory Engineering Processing By-Products, Proceedings of the XVI Congress of the International Society of Sugar Cane Technologists* (São Paulo, Brazil, 9-25 September 1977). Cia Brasileira de Impressão e Propaganda, 1978, pp. 2847-2858.

Aguilar, J. R., G. Arroyave, and M. Flores. Fortificación de azúcar con vitamina A – Una estrategia eficaz para el control de la hipovitaminosis A. Paper presented at the I Latin American Congress of the World Council for the Well-being of the Blind (São Paulo, Brazil, 9-14 October 1977).

Mejia, L. A., R. E. Hodges, G. Arroyave, et al. Vitamin A deficiency and anemia in Central American children. *Am J Clin Nutr* 20:1175-1184, 1977.

Arroyave, G. Control of vitamin A deficiency; fortification of sugar with vitamin A. Part II. *Sugar y Azúcar* 72(8):36-37, 40, 1977.

Arroyave, G. Sobre la fortificación de azúcar con la vitamina A – Un informe sobre este desarrollo en Guatemala. Parte II. *Sugar y Azúcar* 72(8):67-69, 1977.

Arroyave, G., and M. Calcaño. Disminución de los niveles séricos de retinol durante las infecciones. *Arch Latin Nutr*, 1979. In press.

*Courses and Teaching Seminars*

Aguilar, J. R. Participation in the training course on vitamin A, sponsored by the International Eye Foundation (Washington, D.C., February-March 1977).

Arroyave, G. Participation in the Seminar on Hypovitaminosis A in Brazil (Recife, Brazil, 27-29 September 1977).

Arroyave, G., and J. R. Aguilar. Ten presentations to Government officials and staff of the sugar industry in Costa Rica, El Salvador, Guatemala, Honduras, and Panama, 1976-1977.

Numerous lectures to students.

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| No. 350 | Enterotoxigenic *Clostridium perfringens* Type A in Selected Humans. I. A Prevalence Study, por M. J. Torres-Anjel, H. P. Riemann y C. C. Tsai. 1977 (35 pp.) | 2.00 |
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| No. 348 | The Role of the Nurse in Primary Health Care. 1977 (20 pp.) | 1.00 |
| No. 348 | El papel de la enfermera en la atención primaria de salud. 1977 (20 págs.) | 1.00 |
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