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March 20, 1969

Dr. Martin J. Forman
WOH/NCF
Room C-630, SA-10
Agency for International Development
Washington, D. C. 20523

Re: Contract No. AID/csd-2170

Dear Marty:

Our "team" returned from Thailand on February 24, and you will find a half dozen copies of our report enclosed.

From this report you will see that our idea of an orphanage study (Phase III) as originally described is not feasible. On the other hand, we think a somewhat similar study using preschool children in villages is feasible. Further, by conducting Phase III in villages (referred to as Revised Phase III) rather than orphanages, we will at the same time be able to make a number of studies all related to the feasibility of a large scale village field study, Phase IV of the original proposal.

Thus, we think that what we have described in the enclosed report as Revised Phase III is in keeping with the intent of the original Phase III and since we can do it within the same time and budget of the original Phase III we propose to do so. I would appreciate a brief note from you that this meets with your approval.

Actually, I think our month in Thailand was a great success, much more so than I had anticipated. We and our Thai counterparts - Dr. Amorn Nondasuta and Mr. Uthai Pisolyabutra - meshed very well. I am certain they are anxious to have us do this study, and we should be pleased to work with them.

You may know that I will be in Washington next Wednesday (March 26) for a 9 a.m. meeting with Dr. Curtis to talk about a study in Tunisia with wheat fortification. This looks very promising and can be started immediately if funded. Perhaps you will be at this meeting and, if so, maybe we can chat about the Thai study. If you have any questions let me know, and as soon as I have word from you that our Revised Phase III meets with your approval as long as we stay within the funds allocated for Phase III, we will be in business.

With kind regards,

Sincerely,

Fredrick J. Stare

enclosures

March 19, 1969

Report on Phase I

of

Nutritional Improvement of Rice by Fortification with Synthetic Amino Acids, Vitamins, and Iron

by

Fredrick J. Stare, M.D.
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Robert B. McGandy, M.D.

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and

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Part 1 - Nutrition

Part 2 - Economics

Part 3 - Appendix

Contract No. AID/csd - 2170

Nutritional Improvement of Rice by Fortification with Synthetic Amino Acids and Vitamins

Part 1

Introduction

Rice nourishes more of mankind than any other single food, but milled rice by itself is deficient in several essential nutrients. It is low in protein content and in two essential amino acids--lysine and threonine. Protein malnutrition commonly develops in young children living largely on rice. In mild stages this may be manifested only by poor growth and development whereas more extreme and prolonged protein deficiency will result in kwashiorkor-like disease syndromes. Polished rice is deficient in thiamine and vitamin A, hence beriberi and xerophthalmia frequently develop in populations whose primary food is rice.

Fortification of rice with thiamine has been done "off and on" during the past twenty years, and the virtual elimination of beriberi from the Bataan Penninsula in the Philippines, is of course a classic example of improved public health via the fortification of rice. Unfortunately this fortification has not been continued with the result that beriberi has returned in those areas where it was terminated.

For many years it has been known that the quality of rice protein can be enhanced substantially through the addition of lysine and threonine. It has also been shown that for many rice eating peoples, particularly those of the lower economic classes, rice is essentially their sole source of protein. This is most unfortunate during the weaning period, during which time a deficit in protein has its most marked effect.

It is generally accepted by nutritionists, physicians, and public health workers in Thailand that there is a need for improving the protein nutriture of the Thai people. As elsewhere, however, there is little agreement as to how this can best be accomplished, and most economically.

Protein supplementation programs, genetic improvement of rice in terms of yield, protein content and quality, and efforts to stimulate fish and chicken culture are examples of approaches already under way in Thailand.

Major deterrents in the practical application of fortifying rice protein with synthetic amino acids have been the expense of the amino acids, and the means of incorporating and retaining the amino acids as well as any other water soluble nutrients that may be included in the fortification mix. Evidence is also lacking to demonstrate that the improvement obtained by fortification with amino acids is sufficient to be of practical significance in alleviating protein malnutrition. Recently, new products have been developed by a number of commercial companies. These products simulate polished rice in shape and appearance. This "rice pill" has been designed to maintain its structure throughout the various cooking procedures used with rice, yet the nutrients should become available during digestion. Such "pills", simulating rice grains, may be made with a relatively high content of amino acids. Other nutrients needed in small amounts could likewise be included.

The Department of Nutrition of the Harvard School of Public Health proposes to study the effect of fortifying rice diets with lysine and threonine, the two amino acids limited in rice protein. In some of these studies the simultaneous fortification of rice with thiamine, vitamin A and iron will also be evaluated.

The use of the "rice pill" provides a new mechanism for introducing these nutrients into the diets of rice eaters <u>without changing their food habits</u> or altering their customs. Thus, this approach to the improvement of protein nutriture of rice eaters differs substantially from all previous attempts to effect this extremely important public health measure.

Our initial proposal was divided into four phases:

Phase I, a planning stage, which has just been completed, consisted of a four week visit to Thailand by three representatives of Harvard's Department of Nutrition: Dr. S. N. Gershoff, an associate professor and a nutritional biochemist; Dr. R. B. McGandy, an associate professor and a physician-nutritionist-epidemiologist; Dr. M. M. Wagner, an associate professor, University of Illinois and an agricultural economist. This phase was designed to determine what kind of research programs relative to amino acid fortification were feasible in Thailand. During their last week in Thailand the team was joined by Dr. F. J. Stare, Chairman of the Department of Nutrition at Harvard's School of Public Health. Enthusiastic cooperation and assistance were provided the Harvard team by Dr. Amorn Nondasuta, Director, and Mr. Uthai Pisolyabutra, senior nutritionist, of the Thai Division of Nutrition in the Department of Health. Enclosed is a detailed agenda of the Harvard team's activities during its four-week study. As can be seen from this agenda, Phase I involved visits to institutions, villages, day care centers, health centers and conversation with essentially all professional and administrative personnel in Thailand who are interested in or have authority for the conduct of nutrition studies or programs in Thailand.

Phase II - studies with experimental animals.

During the past several months and even as this report is being written, studies are being conducted in the Boston laboratories of the Harvard Department of Nutrition by Dr. D. M. Hegsted, Professor of Nutrition. This phase has been designed to determine the amounts of lysine and threonine which provide optimal growth stimulation when added to rat diets whose sole source of protein is provided by Thai rice. Milled rice from proposed test villages in Thailand was brought back to Harvard at the end of Phase I for futher studies. Since in these studies free lysine and/or threonine are being added to rat diets, Phase II studies will

include investigations of the availability of the amino acids added in the form of rice pills. The amount of amino acids to be used in the rice pills will be based on the results of these investigations.

Phase III - institutional studies with children.

A major aim of the team visit to Thailand was to ascertain whether controlled clinical trials on pre-school children in institutions or orphanages could be carried out. It was hoped that such studies could provide an intermediate assessment of the biological effectiveness of rice fortification - studies somewhere between animal investigations on the one hand and a full scale village field trial on the other.

It was the opinion of the Harvard team that the excellent diets and general care received by institutionalized Thai pre-school children precludes their use in any type of amino acid or other nutrient fortification or supplementation studies. However, we do believe that somewhat similar studies can be done in village day care centers with pre-school children. These will be described later in this report.

Phase IV - large scale field studies.

Clearly, there are important questions to be answered before large scale field studies can be undertaken. On the basis of the consultations and visits of the Harvard team, it was concluded that studies on the effects of amino acid fortification of rice are indeed feasible in Thai villages. Because the design of such an undertaking involves many methodological problems, we are suggesting that Phase IV studies be preceded by an altered Phase III study plan, an alteration that will use day care centers instead of orphanages and will begin to gather information relative to the eventual Phase IV program of a field study.

Protocol for Phase III (Revised)

The Thai Health Department has started the development in several villages of what they call Day Care Centers. These consist of a simple one room thatch-covered building measuring somewhere around 25 feet square with usually no side walls. It is a sheltered play area with opened fenced space around it. It serves as a place where village pre-school children from 2 to 5 or 6 years of age can be taken at 8 a.m., left for the day, and picked up in mid- to late afternoon and taken home. This makes it possible for young children to be cared for "during the day" while the rest of the household may be working.

These Day Care Centers may have anywhere from 10 to 90 children depending on the size of the village and their acceptability by the villagers. The Health Department provides the materials, but the villagers themselves provide the labor and construct the Centers. The Centers are attended by one or two mothers and they are given guidance by a supervisor or attendant who has been given training by Health Department personnel.

In the Centers the pre-school children get some instruction in play, are taught to wash their hands before eating, brush teeth, sing songs, etc. and they are provided with lunch. The food for lunch consists mostly of rice and is brought in the morning from home with the child. In a few Day Care Centers the Thai Health Department is providing various nutritional supplements.

The Day Care Centers serve as a central point to reach most of the village pre-school children. They are readily available in one place for immunization procedures. We intend to use the Day Care Center (rather than orphanages as originally suggested) to test the acceptability of our fortified rice with pre-school children and to carry out certain studies as will be described

later in this report. We think the information will be more meaningful to the ultimate design and carrying out of a field study as envisaged in Phase IV than the original idea of an orphanage study.

In addition to the studies with pre-school children we will test the practicality of carrying out the Phase IV field study in practical village situations. While we feel confident that we can locate villages with discrete, well-defined rice supplies and with only one or two small mills serving the entire population, the major questions to be answered are:

1. Can the cooperation of the millers be obtained for this type of program?

2. Can the artificial rice grains be successfully, reliably, and consistently introduced at the village mill?

3. Will this kind of program be acceptable to village populations for a year or more?

4. Are the nutrients of the rice pill stable, available, and not lost in any appreciable quantity during cooking procedures?

The Revised Phase III pilot study will be the model, in terms of both logistics and costs, for future expansion to a full scale, definitive field trial as envisaged for Phase IV. In itself, the revised Phase III study with children in Day Care Centers will be neither large enough nor of long enough duration to lead to any valid conclusions as to the effect of rice fortification on health, though measurements will be made in part to assess the cooperation of children and parents.

During the first six month period, representative samples of both cooked and uncooked rice will be obtained from village households. It is hoped that arrangements can be made with the School of Medicine or the Anemia Malnutrition

Research Center in Chiengmai for the analysis in one of their laboratories of certain nutrients. Occasional samples will be preserved according to ICNND methods and taken to the laboratories of the Division of Nutrition, Thai Health Department, Bangkok, and also shipped to the Harvard laboratories in Boston as checks on the analysis in Chiengmai, for analysis of: lysine, threonine, vitamin A, thiamine, and iron.

At approximately six months after the actual onset of this pilot fortification study, we believe we can make a preliminary decision on the logistic feasibility of a full Phase IV trial. At that time, studies designed to select matched villages for Phase IV will be initiated by our associates in the Thai Division of Nutrition and ourselves. In each of several different geographic areas of Thailand, villages will be examined for demographic data, sources of rice and food supply, age-specific heights and weights of young children, and desire to cooperate. This will help provide the basis for selecting comparable villages in each area for Phase IV studies.

Materials and Methods

1) The artificial rice grain:

a) The provisional formulation, per artificial rice grain is as follows:

10 micrograms thiamine

4 micrograms vitamin A

0.1 milligrams of iron as ferrous sulfate

In addition to these nutrients, grains for the full test area will contain:

4 milligrams L-lysine

2 milligrams L-threonine

Assume that 50 gm of Thai rice contains 2600 rice grains, each grain

weighs 20 mg. Assume 20 mg as the weight of an artificial grain (rice pill) also.

As a mixing ratio of 1 artificial per 200 grains real rice, a child receiving 250 gm of rice daily will thus receive 65 pellets of artificial rice which will furnish: 0.65 mg thiamine

866 I.U. vitamin A

6.5 mg of iron

plus, in the test area:

0.25 gm of extra lysine

0.13 gm of extra threonine

These suggestions are subject to change depending on the results of the ongoing studies of Phase II.

b) Method of introduction into rice supply: In order to insure even distribution of the artificial rice grains into the rice supply of the villages, a machine to add the "pills" to the rice as it leaves the mill will be developed by the Division of Farm Mechanization, Department of Rice, Ministry of Agriculture. The team has received assurance that such machines could be designed and constructed in a relatively short time for any type of mill.

2) The characteristics of the villages:

a) Villages for revised Phase III will be selected by the Thai Division of Nutrition on the evidence of retarded physical growth and development among pre-school children as compared with standards developed by the Division of Nutrition for pre-school children in better health and living in villages in the Chiangmai area.

b) Villages for revised Phase III will be chosen in northern Thailand in the vicinity of Chiengmai. They will be villages which are relatively isolated,

essentially self-sufficient in rice, and in each of which the rice is milled in no more than two local mills.

c) The population of each village will be between 400 to 800 persons--about 60 to 120 pre-school children (1-5 years old).

d) The villages chosen will not have the direct services of physician, nurse, or sanitarian, although district midwife service will be available. All pre-school children will have been vaccinated and given routine immunizationa by the district midwife.

e) It should be pointed out that the selection of villages for the proposed revised Phase III pilot study will be based primarily on convenience in doing this methodologic trial. In selecting villages for Phase IV studies, considerable thought and effort must be made to assure comparability, to define initial nutritional and health status of the population as well as geographic, economic and social factors.

3) The Day Care Center:

The establishment of a Day Care Center in each of the villages will be the major means for obtaining village cooperation in these studies, and for rendering a needed and visable manifestation of our good intentions. With the Division of Nutrition's protein supplement studies, such centers have been very successful. For purposes of this study, of course, the food served at the Day Care Center will be the usual local foods supplied by the parents rather than special supplements--these centers will thus be very similar to the "control villages" used in the Division's present protein supplement studies. Day Care Centers are very moderate to build and to maintain. Mothers help in their operation and assist the Day Care Center aid. Furthermore, the Day Care Center itself becomes a convenient gathering point for the periodic clinical examinations.

All pre-school children, regardless of whether they participate in the center will be followed up. We feel that the use of Day Care Centers for the study of the pre-school child is a more realistic approach to the feasibility of rice fortification than the original Phase III utilizing orphanages.

4) Assessment of the fortification program:

In this pilot study, height, weight and skin fold thickness will be the primary end point measurements. We further propose to measure hemoglobin and hematocrit levels among pre-school and school children in these villages near the beginning, during the midpoint, and near the end of this twelve month program.

More elaborate biochemical studies will not be undertaken at present, nor will estimates of other health parameters be attempted for the pilot studies, e.g.: height and weight of school aged children; birthweights of newborn babies; mortality in the pre-school age group; detailed biochemical and clinical evaluation of nutrition status. As stated earlier these various procedures are really not to test the value of fortification, but to test the reaction and cooperation of the people to these tests that will be needed for Phase IV.

5) The experimental design:

Four villages will be allocated as follows:

	Village 1	2	3	4
Day Care Center	Yes	Yes	Yes	No
Rice pellets in village rice supply: thiamine, vitamin A, iron	Yes	–	–	–
Rice pellets in village rice supply: thiamine, vitamin A, iron, lysine, threonine	–	Yes	–	–
Rice pellets in village rice supply: placebo only - no nutrients	–	–	Yes	–

Height (to the nearest 0.5 cm), weight (to the nearest 0.1 kg), and triceps skin fold thickness will be measured during the baseline, pretrial period and at six and twelve months after onset of the study program. These measurements will be made on all village children initially in the 1-5 age group.

This design, applied to a large scale trial, will allow for comparison of the effect of thiamine, vitamin A, and iron alone and of these nutrients plus lysine and threonine. Village 3 will allow for an assessment of any possible "Day Care Center effect" on health of pre-school children. Village 4 will serve as a raw control with no intervention aside for the scheduled growth and development measurements.

Economic Aspects of the Feasibility of Rice Fortification

Melvin M. Wagner[1]

Part 2

During the period January 15 - February 14, 1969, the author served as the agricultural economist on a Harvard University team in Thailand studying the feasibility of fortifying rice with an artificial rice pellet containing two amino acids, lysine and threonine, and certain vitamins and minerals. This report presents the author's findings and views concerning the economic aspects of the proposed rice fortification project.

The high correlation between income levels on the one hand and physical stature, health, and longevity on the other is well known; it has been demonstrated in most North American, European, and Oceanic countries and is currently being demonstrated in Japan in connection with that country's post-war prosperity. This correlation no doubt reflects, among other things, the very close relationship between income and expenditures on wider varieties of foods and higher proportions of more nutritious (and more expensive) foods such as meats and vegetables.

For about two-thirds of the world's population, however (of which about half live in India, Pakistan, Mainland China, and Indonesia), it may be some decades before substantial progress in improving nutritional levels is made if it must depend upon rising incomes alone; for while at present rates a decade or more is required just to double incomes in most developing countries, increases of several fold would be required in most to achieve even the current income level of Japan. Thus, the fact that it is now technologically possible to fortify rice with a combination of synthetic lysine, threonine, and vitamins and minerals produced at a cost of about $2.00 per year per person supplied is exciting; for

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[1]Associate Professor of Agricultural Economics, University of Illinois, on leave of absence for one month to work with the Harvard Nutrition team in Thailand.

it raises the possibility of substantially increasing nutritional levels at a cost which, using Thailand as an example, would represent the equivalent of only one to two per cent of that country's current income.

The research project which is now being proposed has as its basic objective the determination of the biological and physiological effects of the introduction of the synthetic rice pellet into the diet of people living under normal village conditions. What follows is limited to a discussion of some of the economic costs and problems which might be involved both in the research project and in any large-scale fortification project which might follow, and of the shape which studies of the economic feasibility of possible large-scale projects might take.

Pellet Cost

Basically, the cost of producing the rice fortification pellets should not be much greater than the cost of the active ingredients and the binder required to make them. The amino acids lysine and threonine, which will constitute about 30% of the pellet will probably represent the major portion of its cost[1]. Vitamins and minerals will comprise a very small proportion of both the pellet and its cost. The remaining two-thirds of the pellet will consist of the binder (rice flour or corn starch) required to hold it together, for which costs would also be low. Beyond ingredients, an additional cost is involved in the extrusion process required to combine the ingredients into pellet form. Total costs for producing the rice fortification pellet are currently estimated by the supplier at $2.50 per kilogram.

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[1]Synthetically-produced lysine is apparently proving to be economically more efficient in meeting the requirements for that amino acid in livestock production than lysine from natural sources. Since there is little difference in the production of lysine for human and animal consumption (one additional purification process is required to meet standards for human consumption), this enhances prospects for future cost reductions based on very large production.

Pellet Dispensing Devices

In any fortification program, there would be a capital cost associated with equipping rice mills with a device for dispensing the pellets into the rice at the required rate at the end of the rice milling process. Dispensing machines for large-type rice mills are said to be available for $300 each. None appropriate for small mills, estimated to comprise more than 20,000 of Thailand's total of 23,000 mills, are known to exist.

The author discussed the problem of a dispensing device with Mr. M. R. Debaridhi Devakul, Special Agricultural Officer in the Department of Rice, Ministry of Agriculture, RTG (who has his offices as Kasetsart University). M. R. Debaridhi agreed to undertake the design of a device for small mills if needed, and estimates that prototype dispensers for each type of mill which might be found in the pilot villages would cost about $500 each.

It is impossible at this point to estimate closely the cost of equipping all of Thailand's rice mills with dispensers if they were mass-produced. As mentioned, machines for large mills are said to be available for about $300. The cost of a mass-produced machine appropriate for small mills would depend, among other things, upon the accuracy required in dispensing the pellet. The expectation is that the pellet would be added at the rate of one per 200 grains of rice; assuming fifty grains of rice per gram, a child consuming 250 grams of rice per day should receive 65 pellets per day. (Total average per capita consumption of rice in Thailand is about 400 grams per day, which would imply an average requirement of 100 pellets per person per day.) If some margin of error could be tolerated so that a very simple device for dispensing the pellet would suffice, such a device for small rice mills might cost no more than $50 each in mass production. If so, the capital cost of dispensing devices for all the mills in

Thailand, both large and small, would be less than five cents per person per year even if depreciated completely in one year.

In the author's discussions with M. R. Debaridhi, he learned of a newly-developed small rice mill which could offer the possibility for considerable savings on some protion of the dispensing devices which would be required in any eventual large scale program. The Division of Farm Machinery of the Department of Rice has just completed designing and is currently testing a new mobile rice mill capable of milling two tons of rice per day (an amount equivalent to the rice needs of an average-sized village of 400 persons for 12 days). The mill has several advantages over those currently in use. First, since it is mobile and uses a tractor as its power source, it would be possible to mill the rice for up to twelve average-sized villages with one mill. Second, the mill separates rice hulls from the grain by centrifugal force, relying on the fact that the rice grain is much heavier than the hull; and this method is said to result in less breaking off of endosperms than methods used in other machines. Third, although the mill is small, it uses the same process for polishing the rice that has previously been used only in large mills, a process which results in relatively fewer cracked grains. Fourth, the rice hulls and the bran are separated in the milling process, and the rice itself passes through a simple grading device which separates it into two grades. Given these characteristics, the new mobile mill would seem to have a good chance for success.

The designer, M. R. Debaridhi, has estimated that the mobile mill could be produced commercially for less than $500 If the mill is successful, only 6,000 to 7,000 of them would be required to meet the entire rice needs of the villagers of Thailand, compared with the more than 20,000 small mills currently in use. If a device for dispensing fortification pellets could be incorporated into

this mill before commercial production is started, the cost would no doubt be lower than for fitting a dispensing device onto an already operating mill. Furthermore, if the mill is as successful as some of the other machines designed by M. R. Debaridhi, it might very well eventually be distributed throughout Asia, including in areas where home milling is now so dominant as to practically preclude a reliable fortification scheme.

Distribution Costs

Fortifying the diet of a population, as opposed to supplementing it, offers considerable advantage in that success does not depend upon changing the eating habits of the population nor upon educating mothers to change their habits of meal preparation. It cannot be emphasized too strongly that the advantage is economic as well as otherwise; as experience in the area of agricultural extension has repeatedly demonstrated, the economic costs, both direct and indirect, of trying to reach and persuade even a significant proportion of a population to take a particular action are great indeed.[1]

Even in a fortification program, however, the promotion and distribution of pellets would of course involve costs. Promotion costs would differ substantially depending upon the degree of support for fortification which might be received from the government, and upon the extent to which the costs of fortification were passed on to the consumer and in what way (e.g. whether or not it tended to foster consumer resistance). Distribution costs would depend, among other things, upon whether channels already existing for some other product might be utilized. These costs are difficult to project but would perhaps not exceed 50% of the cost of producing the pellet.

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[1]The indirect costs may be even greater than the direct ones. One of the author's conclusions on the basis of his five years of experience in Thailand is that, contrary to popular opinion, most government officials already have more than they can do effectively and take on new tasks only at considerable cost to existing assignments.

Total Costs

If a reasonably simple and efficient distribution and promotion system can be designed, a very rough estimate of the total cost of fortifying human diets with the amino acid, vitamin, and mineral pellet would be on the order of $2.50 to $3.00 per person per year, perhaps less if further research indicates the potential for a very large market for lysine and other ingredients involved. $2.50 to $3.00 per person would mean a total cost on the order of about $100 million per year for a country of Thailand's current population. This would amount to less than 2% of the current average disposable personal income of Thais, less than 6% of total expenditures on food, and less than 16% of expenditures on rice.

Comments

If questions concerning levels of nutrition were unrelated to questions of economic efficiency, costs, etc., the solution to many, if not most, nutritional problems would be to increase the variety and quality of foods consumed; but as previously noted, a solution which depends upon rising incomes may well be decades in coming in some, perhaps many, countries. Given that fact, the need for careful economic study of alternative ways of increasing nutritional levels seems obvious; yet an economic evaluation is often a missing element in the many programs under way.

Although present knowledge and techniques preclude really thorough measurement, it is conceptually possible to measure at least some of the output variables (benefits) of improved nutrition; and there is every reason to think that these benefits may be large indeed.[1] Balanced against these benefits would be the costs of accomplishing the same nutritional objectives in alternative ways.

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[1]For example, Lester Brown, in his Man, Land, and Food, notes that the expected years of work life for a baby born in the United States is four times that for a baby born in Northeastern Brazil, with poor nutrition as one basic reason for the difference.

In the author's view, the most useful economic evaluation of any large-scale program which might evolve from the present project would be one which involved both an analysis of the costs which would be involved in a fortification scheme of the type contemplated here and a comparison of costs and expected benefits among programs with similar nutritional objectives.

Appendix
Part 3

Program of consultations, site, and project visits
For the Harvard Team during the month of Phase I;
Arranged by the Division of Nutrition, Department of
Health:

Dr. Amorn Nondasuta, Director
Mr. Uthai Pisolyabutra, Senior Nutritionist

Dr. Somboon Pon Aksara, Under Secretary of State for Public Health

Dr. Prachoom Indram Barya, Deputy Director General of Health

Dr. Mali Thainue, Deputy Director General of Health

Dr. Sutham Hiraya Narumol, Provincial Health Office, Chiengmai

Dr. Sala Thasanenda, Director General of Rice Department, Ministry of Agriculture

Mr. Sombhoj Suwanavongse, Rice Department, Rice Breeding Institute, University of Kasetsart

Dr. Kanchana Chutima, Department of Chemistry, Kasetsart University

Mr. Chitra, Manager)
) Thai Rice Company
Mr. Boonterm, Assistant Manager)

Dr. Chek Thanasiri, Chief, Municipal Health Office, Bangkok

Dr. Prasongporn Chalumirindha, Chief, Pediatric Division, Municipal Health Office, Bangkok

Mrs. Renee Chetedilek, Director, Division of Child and Youth Welfare, Department of Social Welfare

Mr. Cyril Hunnikin, Food Conservation Engineer, UNICEF

Dr. Aree Valayasevi, Acting Dean, Rama Thibodee Medical School, University of Medical Sciences

Dr. Joe Ray, Professor of Pediatrics, Rockefeller Foundation, University of Medical Sciences

Dr. James Dinning, Rockefeller Foundation, University of Medical Sciences

Dr. Amara Chandarapanond, Head, Department of Nutrition, School of Public Health, University of Medical Sciences

Dr. Smith & Mr. Murphy, USOM, Public Health Division

Dr. Kamdhorn Suvarnakich, Former Director General of Public Health
Former Dean, Faculty of Public Health

Dr. Charas Yamarat, Dean, Faculty of Public Health

Dr. Pradisth Cheosakul, Director, Applied Science Research Institute of Thailand

Mr. M. R. Debaridhi Devakul, Special Agricultural Officer, Department of Rice,
Ministry of Agriculture

Appendix (continued)

Institutions and Municipal Day-Care Centers

Inspection of the three institutions responsible for domicilliary care of pre-school children in Thailand:

1) Central Child Health Center
   Division of Maternity and Child Health
   Nondaburi Province

2) Child Welfare Center
   Phayathi Babies Home, Bangkok

3) Child Welfare Center
   Pakkred Babies Home, Bangkok

Visits to three of the six Day Care Centers for pre-school children operated by the Bureau of Public Health, Bangkok

Visit to the MacKean Leprosarium at Koh Klarng, near Chiengmai - care of children, including pre-school, of leprous parents.

Villages

Village field activities, School of Public Health near Korat - Na Klarng, Ma Klue Mai, Pak Thong Chai.

School of Public Health field demonstration - village, Bangkhen.

Pre-school child centers in villages near Chiangmai - Chombhu, Ban Klarng, Ban O, Kee Lek .

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March 19, 1969

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by

Fredrick J. Stare, M.D.
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Department of Nutrition, Harvard School of Public Health
Boston, Massachusetts

and

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Part 1 - Nutrition

Part 2 - Economics

Part 3 - Appendix

Contract No. AID/c d - 2170

A.I.D.
Reference Center
Room 1656 NS

Nutritional Improvement of Rice by Fortification with Synthetic Amino Acids and Vitamins

Part 1

Introduction

Rice nourishes more of mankind than any other single food, but milled rice by itself is deficient in several essential nutrients. It is low in protein content and in two essential amino acids--lysine and threonine. Protein malnutrition commonly develops in young children living largely on rice. In mild stages this may be manifested only by poor growth and development whereas more extreme and prolonged protein deficiency will result in kwashiorkor-like disease syndromes. Polished rice is deficient in thiamine and vitamin A, hence beriberi and xerophthalmia frequently develop in populations whose primary food is rice.

Fortification of rice with thiamine has been done "off and on" during the past twenty years, and the virtual elimination of beriberi from the Bataan Penninsula in the Philippines, is of course a classic example of improved public health via the fortification of rice. Unfortunately this fortification has not been continued with the result that beriberi has returned in those areas where it was terminated.

For many years it has been known that the quality of rice protein can be enhanced substantially through the addition of lysine and threonine. It has also been shown that for many rice eating peoples, particularly those of the lower economic classes, rice is essentially their sole source of protein. This is most unfortunate during the weaning period, during which time a deficit in protein has its most marked effect.

It is generally accepted by nutritionists, physicians, and public health workers in Thailand that there is a need for improving the protein nutriture of the Thai people. As elsewhere, however, there is little agreement as to how this can best be accomplished, and most economically.

Protein supplementation programs, genetic improvement of rice in terms of yield, protein content and quality, and efforts to stimulate fish and chicken culture are examples of approaches already under way in Thailand.

Major deterrents in the practical application of fortifying rice protein with synthetic amino acids have been the expense of the amino acids, and the means of incorporating and retaining the amino acids as well as any other water soluble nutrients that may be included in the fortification mix. Evidence is also lacking to demonstrate that the improvement obtained by fortification with amino acids is sufficient to be of practical significance in alleviating protein malnutrition. Recently, new products have been developed by a number of commercial companies. These products simulate polished rice in shape and appearance. This "rice pill" has been designed to maintain its structure throughout the various cooking procedures used with rice, yet the nutrients should become available during digestion. Such "pills", simulating rice grains, may be made with a relatively high content of amino acids. Other nutrients needed in small amounts could likewise be included.

The Department of Nutrition of the Harvard School of Public Health proposes to study the effect of fortifying rice diets with lysine and threonine, the two amino acids limited in rice protein. In some of these studies the simultaneous fortification of rice with thiamine, vitamin A and iron will also be evaluated.

The use of the "rice pill" provides a new mechanism for introducing these nutrients into the diets of rice eaters without changing their food habits or altering their customs. Thus, this approach to the improvement of protein nutriture of rice eaters differs substantially from all previous attempts to effect this extremely important public health measure.

Best Available Document

Our initial proposal was divided into four phases:

Phase I, a planning stage, which has just been completed, consisted of a four week visit to Thailand by three representatives of Harvard's Department of Nutrition: Dr. S. N. Gershoff, an associate professor and a nutritional biochemist; Dr. R. B. McGandy, an associate professor and a physician-nutritionist-epidemiologist; Dr. M. M. Wagner, an associate professor, University of Illinois and an agricultural economist. This phase was designed to determine what kind of research programs relative to amino acid fortification were feasible in Thailand. During their last week in Thailand the team was joined by Dr. F. J. Stare, Chairman of the Department of Nutrition at Harvard's School of Public Health. Enthusiastic cooperation and assistance were provided the Harvard team by Dr. Amorn Nondasuta, Director, and Mr. Uthai Pisolyabutra, senior nutritionist, of the Thai Division of Nutrition in the Department of Health. Enclosed is a detailed agenda of the Harvard team's activities during its four-week study. As can be seen from this agenda, Phase I involved visits to institutions, villages, day care centers, health centers and conversation with essentially all professional and administrative personnel in Thailand who are interested in or have authority for the conduct of nutrition studies or programs in Thailand.

Phase II - studies with experimental animals.

During the past several months and even as this report is being written, studies are being conducted in the Boston laboratories of the Harvard Department of Nutrition by Dr. D. M. Hegsted, Professor of Nutrition. This phase has been designed to determine the amounts of lysine and threonine which provide optimal growth stimulation when added to rat diets whose sole source of protein is provided by Thai rice. Milled rice from proposed test villages in Thailand was brought back to Harvard at the end of Phase I for futher studies. Since in these studies free lysine and/or threonine are being added to rat diets, Phase II studies will

include investigations of the availability of the amino acids added in the form of rice pills. The amount of amino acids to be used in the rice pills will be based on the results of these investigations.

Phase III - institutional studies with children.

A major aim of the team visit to Thailand was to ascertain whether controlled clinical trials on pre-school children in institutions or orphanages could be carried out. It was hoped that such studies could provide an intermediate assessment of the biological effectiveness of rice fortification - studies somewhere between animal investigations on the one hand and a full scale village field trial on the other.

It was the opinion of the Harvard team that the excellent diets and general care received by institutionalized Thai pre-school children precludes their use in any type of amino acid or other nutrient fortification or supplementation studies. However, we do believe that somewhat similar studies can be done in village day care centers with pre-school children. These will be described later in this report.

Phase IV - large scale field studies.

Clearly, there are important questions to be answered before large scale field studies can be undertaken. On the basis of the consultations and visits of the Harvard team, it was concluded that studies on the effects of amino acid fortification of rice are indeed feasible in Thai villages. Because the design of such an undertaking involves many methodological problems, we are suggesting that Phase IV studies be preceded by an altered Phase III study plan, an alteration that will use day care centers instead of orphanages and will begin to gather information relative to the eventual Phase IV program of a field study.

Protocol for Phase III (Revised)

The Thai Health Department has started the development in several villages of what they call Day Care Centers. These consist of a simple one room thatch-covered building measuring somewhere around 25 feet square with usually no side walls. It is a sheltered play area with opened fenced space around it. It serves as a place where village pre-school children from 2 to 5 or 6 years of age can be taken at 8 a.m., left for the day, and picked up in mid- to late afternoon and taken home. This makes it possible for young children to be cared for "during the day" while the rest of the household may be working.

These Day Care Centers may have anywhere from 10 to 90 children depending on the size of the village and their acceptability by the villagers. The Health Department provides the materials, but the villagers themselves provide the labor and construct the Centers. The Centers are attended by one or two mothers and they are given guidance by a supervisor or attendant who has been given training by Health Department personnel.

In the Centers the pre-school children get some instruction in play, are taught to wash their hands before eating, brush teeth, sing songs, etc. and they are provided with lunch. The food for lunch consists mostly of rice and is brought in the morning from home with the child. In a few Day Care Centers the Thai Health Department is providing various nutritional supplements.

The Day Care Centers serve as a central point to reach most of the village pre-school children. They are readily available in one place for immunization procedures. We intend to use the Day Care Center (rather than orphanages as originally suggested) to test the acceptability of our fortified rice with pre-school children and to carry out certain studies as will be described

later in this report. We think the information will be more meaningful to the ultimate design and carrying out of a field study as envisaged in Phase IV than the original idea of an orphanage study.

In addition to the studies with pre-school children we will test the practicality of carrying out the Phase IV field study in practical village situations. While we feel confident that we can locate villages with discrete, well-defined rice supplies and with only one or two small mills serving the entire population, the major questions to be answered are:

1. Can the cooperation of the millers be obtained for this type of program?

2. Can the artificial rice grains be successfully, reliably, and consistently introduced at the village mill?

3. Will this kind of program be acceptable to village populations for a year or more?

4. Are the nutrients of the rice pill stable, available, and not lost in any appreciable quantity during cooking procedures?

The Revised Phase III pilot study will be the model, in terms of both logistics and costs, for future expansion to a full scale, definitive field trial as envisaged for Phase IV. In itself, the revised Phase III study with children in Day Care Centers will be neither large enough nor of long enough duration to lead to any valid conclusions as to the effect of rice fortification on health, though measurements will be made in part to assess the cooperation of children and parents.

During the first six month period, representative samples of both cooked and uncooked rice will be obtained from village households. It is hoped that arrangements can be made with the School of Medicine or the Anemia Malnutrition

Research Center in Chiengmai for the analysis in one of their laboratories of certain nutrients. Occasional samples will be preserved according to ICNND methods and taken to the laboratories of the Division of Nutrition, Thai Health Department, Bangkok, and also shipped to the Harvard laboratories in Boston as checks on the analysis in Chiengmai, for analysis of: lysine, threonine, vitamin A, thiamine, and iron.

At approximately six months after the actual onset of this pilot fortification study, we believe we can make a preliminary decision on the logistic feasibility of a full Phase IV trial. At that time, studies designed to select matched villages for Phase IV will be initiated by our associates in the Thai Division of Nutrition and ourselves. In each of several different geographic areas of Thailand, villages will be examined for demographic data, sources of rice and food supply, age-specific heights and weights of young children, and desire to cooperate. This will help provide the basis for selecting comparable villages in each area for Phase IV studies.

Materials and Methods

1) The artificial rice grain:

a) The provisional formulation, per artificial rice grain is as follows: 10 micrograms thiamine

4 micrograms vitamin A

0.1 milligrams of iron as ferrous sulfate

In addition to these nutrients, grains for the full test area will contain: 4 milligrams L-lysine

2 milligrams L-threonine

Assume that 50 gm of Thai rice contains 2600 rice grains, each grain

weighs 20 mg. Assume 20 mg as the weight of an artificial grain (rice pill) also.

As a mixing ratio of 1 artificial per 200 grains real rice, a child receiving 250 gm of rice daily will thus receive 65 pellets of artificial rice which will furnish: 0.65 mg thiamine

866 I.U. vitamin A

6.5 mg of iron

plus, in the test area:

0.25 gm of extra lysine

0.13 gm of extra threonine

These suggestions are subject to change depending on the results of the ongoing studies of Phase II.

b) Method of introduction into rice supply: In order to insure even distribution of the artificial rice grains into the rice supply of the villages, a machine to add the "pills" to the rice as it leaves the mill will be developed by the Division of Farm Mechanization, Department of Rice, Ministry of Agriculture. The team has received assurance that such machines could be designed and constructed in a relatively short time for any type of mill.

2) The characteristics of the villages:

a) Villages for revised Phase III will be selected by the Thai Division of Nutrition on the evidence of retarded physical growth and development among pre-school children as compared with standards developed by the Division of Nutrition for pre-school children in better health and living in villages in the Chiangmai area.

b) Villages for revised Phase III will be chosen in northern Thailand in the vicinity of Chiengmai. They will be villages which are relatively [illegible]

essentially self-sufficient in rice, and in each of which the rice is milled in no more than two local mills.

c) The population of each village will be between 400 to 800 persons--about 60 to 120 pre-school children (1-5 years old).

d) The villages chosen will not have the direct services of physician, nurse, or sanitarian, although district midwife service will be available. All pre-school children will have been vaccinated and given routine immunizationa by the district midwife.

e) It should be pointed out that the selection of villages for the proposed revised Phase III pilot study will be based primarily on convenience in doing this methodologic trial. In selecting villages for Phase IV studies, considerable thought and effort must be made to assure comparability, to define initial nutritional and health status of the population as well as geographic, economic and social factors.

3) The Day Care Center:

The establishment of a Day Care Center in each of the villages will be the major means for obtaining village cooperation in these studies, and for rendering a needed and visable manifestation of our good intentions. With the Division of Nutrition's protein supplement studies, such centers have been very successful. For purposes of this study, of course, the food served at the Day Care Center will be the usual local foods supplied by the parents rather than special supplements--these centers will thus be very similar to the "control villages" used in the Division's present protein supplement studies. Day Care Centers are very moderate to build and to maintain. Mothers help in their operation and assist the Day Care Center aid. Furthermore, the Day Care Center itself becomes a convenient gathering point for the periodic clinical examinations.

All pre-school children, regardless of whether they participate in the center will be followed up. We feel that the use of Day Care Centers for the study of the pre-school child is a more realistic approach to the feasibility of rice fortification than the original Phase III utilizing orphanages.

4) Assessment of the fortification program:

In this pilot study, height, weight and skin fold thickness will be the primary end point measurements. We further propose to measure hemoglobin and hematocrit levels among pre-school and school children in these villages near the beginning, during the midpoint, and near the end of this twelve month program.

More elaborate biochemical studies will not be undertaken at present, nor will estimates of other health parameters be attempted for the pilot studies, e.g.: height and weight of school aged children; birthweights of newborn babies; mortality in the pre-school age group; detailed biochemical and clinical evaluation of nutrition status. As stated earlier these various procedures are really not to test the value of fortification, but to test the reaction and cooperation of the people to these tests that will be needed for Phase IV.

5) The experimental design:

Four villages will be allocated as follows:

	Village			
Day Care Center	[illegible]	[illegible]	[illegible]	[illegible]
Rice pellets in village rice supply: thiamine, vitamin A, iron	Yes	–	–	–
Rice pellets in village rice supply: thiamine, vitamin A, iron, lysine, threonine	–	Yes	–	–
Rice pellets in village rice supply: placebo only - no nutrients	–	–	Yes	–

Height (to the nearest 0.5 cm), weight (to the nearest 0.1 kg), and triceps skin fold thickness will be measured during the baseline, pretrial period and at six and twelve months after onset of the study program. These measurements will be made on all village children initially in the 1-5 age group.

This design, applied to a large scale trial, will allow for comparison of the effect of thiamine, vitamin A, and iron alone and of these nutrients plus lysine and threonine. Village 3 will allow for an assessment of any possible "Day Care Center effect" on health of pre-school children. Village 4 will serve as a raw control with no intervention aside for the scheduled growth and development measurements.

Economic Aspects of the Feasibility of Rice Fortification

Melvin M. Wagner[1]

Part 2

During the period January 15 - February 14, 1969, the author served as the agricultural economist on a Harvard University team in Thailand studying the feasibility of fortifying rice with an artificial rice pellet containing two amino acids, lysine and threonine, and certain vitamins and minerals. This report presents the author's findings and views concerning the economic aspects of the proposed rice fortification project.

The high correlation between income levels on the one hand and physical stature, health, and longevity on the other is well known; it has been demonstrated in most North American, European, and Oceanic countries and is currently being demonstrated in Japan in connection with that country's post-war prosperity. This correlation no doubt reflects, among other things, the very close relationship between income and expenditures on wider varieties of foods and higher proportions of more nutritious (and more expensive) foods such as meats and vegetables.

For about two-thirds of the world's population, however (of which about half live in India, Pakistan, Mainland China, and Indonesia), it may be some decades before substantial progress in improving nutritional levels is made if it must depend upon rising incomes alone; for while at present rates a decade or more is required just to double incomes in most developing countries, increases of several fold would be required in most to achieve even the current income level of Japan. Thus, the fact that it is now technologically possible to fortify rice with a combination of synthetic lysine, threonine, and vitamins and minerals produced at a cost of about $2.00 per year per person supplied is exciting; for

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[1]Associate Professor of Agricultural Economics, University of Illinois, on leave of absence for one month to work with the Harvard Nutrition team in Thailand.

it raises the possibility of substantially increasing nutritional levels at a cost which, using Thailand as an example, would represent the equivalent of only one to two per cent of that country's current income.

The research project which is now being proposed has as its basic objective the determination of the biological and physiological effects of the introduction of the synthetic rice pellet into the diet of people living under normal village conditions. What follows is limited to a discussion of some of the economic costs and problems which might be involved both in the research project and in any large-scale fortification project which might follow, and of the shape which studies of the economic feasibility of possible large-scale projects might take.

Pellet Cost

Basically, the cost of producing the rice fortification pellets should not be much greater than the cost of the active ingredients and the binder required to make them. The amino acids lysine and threonine, which will constitute about 30% of the pellet will probably represent the major portion of its cost[1]. Vitamins and minerals will comprise a very small proportion of both the pellet and its cost. The remaining two-thirds of the pellet will consist of the binder (rice flour or corn starch) required to hold it together, for which costs would also be low. Beyond ingredients, an additional cost is involved in the extrusion process required to combine the ingredients into pellet form. Total costs for producing the rice fortification pellet are currently estimated by the supplier at $2.50 per kilogram.

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[1] Synthetically-produced lysine is apparently proving to be economically more efficient in meeting the requirements for that amino acid in livestock production than lysine from natural sources. Since there is little difference in the production of lysine for human and animal consumption (one additional purification process is required to meet standards for human consumption), this enhances prospects for future cost reductions based on very large production.

Pellet Dispensing Devices

In any fortification program, there would be a capital cost associated with equipping rice mills with a device for dispensing the pellets into the rice at the required rate at the end of the rice milling process. Dispensing machines for large-type rice mills are said to be available for $300 each. None appropriate for small mills, estimated to comprise more than 20,000 of Thailand's total of 23,000 mills, are known to exist.

The author discussed the problem of a dispensing device with Mr. M. R. Debaridhi Devakul, Special Agricultural Officer in the Department of Rice, Ministry of Agriculture, RTG (who has his offices as Kasetsart University). M. R. Debaridhi agreed to undertake the design of a device for small mills if needed, and estimates that prototype dispensers for each type of mill which might be found in the pilot villages would cost about $500 each.

It is impossible at this point to estimate closely the cost of equipping all of Thailand's rice mills with dispensers if they were mass-produced. As mentioned, machines for large mills are said to be available for about $300. The cost of a mass-produced machine appropriate for small mills would depend, among other things, upon the accuracy required in dispensing the pellet. The expectation is that the pellet would be added at the rate of one per 200 grains of rice; assuming fifty grains of rice per gram, a child consuming 250 grams of rice per day should receive 65 pellets per day. (Total average per capita consumption of rice in Thailand is about 400 grams per day, which would imply an average requirement of 100 pellets per person per day.) If some margin of error could be tolerated so that a very simple device for dispensing the pellet would suffice, such a device for small rice mills might cost no more than $50 each in mass production. If so, the capital cost of dispensing devices for all the mills in

Thailand, both large and small, would be less than five cents per person per year even if depreciated completely in one year.

In the author's discussions with M. R. Debaridhi, he learned of a newly-developed small rice mill which could offer the possibility for considerable savings on some protion of the dispensing devices which would be required in any eventual large scale program. The Division of Farm Machinery of the Department of Rice has just completed designing and is currently testing a new mobile rice mill capable of milling two tons of rice per day (an amount equivalent to the rice needs of an average-sized village of 400 persons for 12 days). The mill has several advantages over those currently in use. First, since it is mobile and uses a tractor as its power source, it would be possible to mill the rice for up to twelve average-sized villages with one mill. Second, the mill separates rice hulls from the grain by centrifugal force, relying on the fact that the rice grain is much heavier than the hull; and this method is said to result in less breaking off of endosperms than methods used in other machines. Third, although the mill is small, it uses the same process for polishing the rice that has previously been used only in large mills, a process which results in relatively fewer cracked grains. Fourth, the rice hulls and the bran are separated in the milling process, and the rice itself passes through a simple grading device which separates it into two grades. Given these characteristics, the new mobile mill would seem to have a good chance for success.

The designer, M. R. Debaridhi, has estimated that the mobile mill could be produced commercially for less than $500. If the mill is successful, only 6,000 to 7,000 of them would be required to meet the entire rice needs of the villagers of Thailand, compared with the more than 20,000 small mills currently in use. If a device for dispensing fortification pellets could be incorporated into

this mill before commercial production is started, the cost would no doubt be lower than for fitting a dispensing device onto an already operating mill. Furthermore, if the mill is as successful as some of the other machines designed by M. R. Debaridhi, it might very well eventually be distributed throughout Asia, including in areas where home milling is now so dominant as to practically preclude a reliable fortification scheme.

Distribution Costs

Fortifying the diet of a population, as opposed to supplementing it, offers considerable advantage in that success does not depend upon changing the eating habits of the population nor upon educating mothers to change their habits of meal preparation. It cannot be emphasized too strongly that the advantage is economic as well as otherwise; as experience in the area of agricultural extension has repeatedly demonstrated, the economic costs, both direct and indirect, of trying to reach and persuade even a significant proportion of a population to take a particular action are great indeed.[1]

Even in a fortification program, however, the promotion and distribution of pellets would of course involve costs. Promotion costs would differ substantially depending upon the degree of support for fortification which might be received from the government, and upon the extent to which the costs of fortification were passed on to the consumer and in what way (e.g. whether or not it tended to foster consumer resistance). Distribution costs would depend, among other things, upon whether channels already existing for some other product might be utilized. These costs are difficult to project but would perhaps not exceed 50% of the cost of producing the pellet.

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[1]The indirect costs may be even greater than the direct ones. One of the author's conclusions on the basis of his five years of experience in Thailand is that, contrary to popular opinion, most government officials already have more than they can do effectively and take on new tasks only at considerable cost to existing assignments.

Total Costs

If a reasonably simple and efficient distribution and promotion system can be designed, a very rough estimate of the total cost of fortifying human diets with the amino acid, vitamin, and mineral pellet would be on the order of $2.50 to $3.00 per person per year, perhaps less if further research indicates the potential for a very large market for lysine and other ingredients involved. $2.50 to $3.00 per person would mean a total cost on the order of about $100 million per year for a country of Thailand's current population. This would amount to less than 2% of the current average disposable personal income of Thais, less than 6% of total expenditures on food, and less than 16% of expenditures on rice.

Comments

If questions concerning levels of nutrition were unrelated to questions of economic efficiency, costs, etc., the solution to many, if not most, nutritional problems would be to increase the variety and quality of foods consumed; but as previously noted, a solution which depends upon rising incomes may well be decades in coming in some, perhaps many, countries. Given that fact, the need for careful economic study of alternative ways of increasing nutritional levels seems obvious; yet an economic evaluation is often a missing element in the many programs under way.

Although present knowledge and techniques preclude really thorough measurement, it is conceptually possible to measure at least some of the output variables (benefits) of improved nutrition; and there is every reason to think that these benefits may be large indeed.[1] Balanced against these benefits would be the costs of accomplishing the same nutritional objectives in alternative ways.

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[1]For example, Lester Brown, in his Man, Land, and Food, notes that the expected years of work life for a baby born in the United States is four times that for a baby born in Northeastern Brazil, with poor nutrition as one basic reason for the difference.

In the author's view, the most useful economic evaluation of any large-scale program which might evolve from the present project would be one which involved both an analysis of the costs which would be involved in a fortification scheme of the type contemplated here and a comparison of costs and expected benefits among programs with similar nutritional objectives.

Appendix
Part 3

Program of consultations, site, and project visits For the Harvard Team during the month of Phase I; Arranged by the Division of Nutrition, Department of Health:

Dr. Amorn Nondasuta, Director
Mr. Uthai Pisolyabutra, Senior Nutritionist

Dr. Somboon Pon Aksara, Under Secretary of State for Public Health

Dr. Prachoom Indram Barya, Deputy Director General of Health

Dr. Mali Thainue, Deputy Director General of Health

Dr. Sutham Hiraya Narumol, Provincial Health Office, Chiengmai

Dr. Sala Thasanenda, Director General of Rice Department, Ministry of Agriculture

Mr. Sombhoj Suwanavongse, Rice Department, Rice Breeding Institute, University of Kasetsart

Dr. Kanchana Chutima, Department of Chemistry, Kasetsart University

Mr. Chitra, Manager)
) Thai Rice Company
Mr. Boonterm, Assistant Manager)

Dr. Chek Thanasiri, Chief, Municipal Health Office, Bangkok

Dr. Prasongporn Chalumirindha, Chief, Pediatric Division, Municipal Health Office, Bangkok

Mrs. Renee Chetedilek, Director, Division of Child and Youth Welfare, Department of Social Welfare

Mr. Cyril Hunnikin, Food Conservation Engineer, UNICEF

Dr. Aree Valayasevi, Acting Dean, Rama Thibodee Medical School, University of Medical Sciences

Dr. Joe Ray, Professor of Pediatrics, Rockefeller Foundation, University of Medical Sciences

Dr. James Dinning, Rockefeller Foundation, University of Medical Sciences

Dr. Amara Chandarapanond, Head, Department of Nutrition, School of Public Health, University of Medical Sciences

Dr. Smith & Mr. Murphy, USOM, Public Health Division

Dr. Kamdhorn Suvarnakich, Former Director General of Public Health
Former Dean, Faculty of Public Health

Dr. Charas Yamarat, Dean, Faculty of Public Health

Dr. Pradisth Cheosakul, Director, Applied Science Research Institute of Thailand

Mr. M. R. Debaridhi Devakul, Special Agricultural Officer, Department of Rice,
Ministry of Agriculture

Appendix (continued)

Institutions and Municipal Day-Care Centers

Inspection of the three institutions responsible for domicilliary care of pre-school children in Thailand:

1) Central Child Health Center
   Division of Maternity and Child Health
   Nondaburi Province

2) Child Welfare Center
   Phayathi Babies Home, Bangkok

3) Child Welfare Center
   Pakkred Babies Home, Bangkok

Visits to three of the six Day Care Centers for pre-school children operated by the Bureau of Public Health, Bangkok

Visit to the MacKean Leprosarium at Koh Klarng, near Chiengmai - care of children, including pre-school, of leprous parents,

Villages

Village field activities, School of Public Health near Korat - Na Klarng, Ma Klue Mai, Pak Thong Chai,

School of Public Health field demonstration - village, Bangkhen,

Pre-school child centers in villages near Chiangmai - Chombhu, Ban Klarng, Ban O, Kee Lek .

Appendix 2

5

Progress Report - April 1970
Harvard-Thailand Rice Fortification Project
Contract No. AID/csd-2170

In February 1970 Dr. Stanley Gershoff and Dr. Robert McGandy went to Thailand to review the progress of Phase III and initiate preparations for Phase IV of the Harvard-Thailand Rice Fortification Project. As previously reported, the rate of progress attained, the cooperation of the Thai officials and technicians, and the attitudes of the people in the experimental villages have been so good that we are very pleased with the development of this study.

In January feeding of the rice fortification grains (RFG) was started in the Pilot Villages. The villages have been treated in the following ways:

1. Raw Control - no intervention except for surveys.
2. Placebo Control - day-care center & placebo RFG.
3. Restricted Treatment - day-care center & RFG containing thiamine, vitamin A and ferric phosphate.
4. Full treatment - day-care center & RFG containing thiamine, vitamin A, ferric phosphate, lysine and threonine.

The day care centers have been very well received. They are not places providing only custodial care. They are being operated more like nursery schools. Although the day-care centers do not provide food, they may have a nutritional effect because it appears that lunches being brought to the center may be better than the children would receive at home if they ate without observation by children from other families. We are excited by the possible health value of the day-care centers and shall carefully look at their impact on our study to determine whether it will be necessary

to put a fifth group in Phase IV, villages receiving the full RFG but no day-care center.

Before the feeding of the RFG was started the pre-school children of the villages were given a clinical examination as previously described, had a hand-wrist X-ray taken, had a fecal parasite examination made, and had blood and urine samples taken for hemoglobin, hematocrit and urinary thiamine and creatinine analyses. Some of the data of these examinations are summarized below.

It can be seen from the two charts that heights and weights of the village children are considerably below the 50th percentile of the Iowa standards. From an assortment of available Thai studies we have put together some height and weight means of middle class Bangkok children. Growth in the villages appears considerably poorer than in this Bangkok group. It can also be seen that head circumferences of the Chiang Mai village children are much smaller than of Iowa children of the same ages. We plan on having all of the hand-wrist x-rays evaluated by an expert here in Boston. However, the evaluation of the x-rays obtained by the Professor of Radiology in Chiang Mai indicates that 26% of the children examined showed delayed bone growth compared to American standards. Mean hemoglobin and hematocrit values in the children examined appeared normal. This is probably related to the fact that intestinal parasites were detected in only about 10% of them.

The RFG feeders which were constructed are working satisfactorily and the millers have been very cooperative. We have representatives of the Division of Nutrition of the Thai Ministry of Health in each village each day to make sure that the RFG is being added properly to the rice as it is milled. Records of the total amount of rice milled daily in each

mill and the amount of RFG used support their reports that the addition of RFG to the rice is proceeding as desired. Analyses of the village rice, treated and untreated with RFG are being made for total protein, lysine, and threonine, at the laboratories of the Division of Nutrition in Bangkok.

We have been very pleased with the cooperation we have received from the radiologists, parasitologists, and the provincial health officers in Chiang-Mai. They have assured us that they would be able to continue to satisfy our needs even if we do the entire full field study in the Chiang-Mai area. Because of this and because we wish to minimize our future logistic problems, we have decided to alter our original plans and do all of Phase IV in the Chiang Mai area.

A resurvey of the four villages is scheduled for June, 1970. In August we shall evaluate the entire pilot study and make definite plans for the full field study of Phase IV. To expedite matters we are currently looking for about 20 more villages suitable for this study. We shall try to locate the additional personnel needed for Phase IV but we shall not hire anybody until our contract has been extended. We shall probably have additional feeders made since they are custom built and we do not want to run the risk of holding up Phase IV because they are not available.

In August, assuming that the pilot study remains satisfactory, we shall make definite plans for building day-care centers, hiring personnel, buying equipment, and obtaining the cooperation of the village officials and millers. This would enable us to start Phase IV in January of 1971.

Our experiences to date have clearly shown the advantages of doing pilot studies before launching into full field studies. Although we have been working under what we believe must be ideal conditions, enough minor problems have arisen so that if Phase IV was being done now instead

of Phase III we would be less satisfied than we are. Fortunately, all of these problems have been minor and will be corrected before Phase IV begins. The following are examples of these difficulties.

Having finally gotten the Ajinomoto Co. to prepare a RFG which looked like rice, cooked like rice and did not alter the taste of rice, we were unable for almost two months to import it into Thailand because there is a law against importing rice and the customs department had to be convinced that it was not rice.

We have had problems in the field with the RFG, particularly the RFG containing the amino acids. Under the environmental conditions in which they must be stored they tend to cake. The Ajinomoto Co. was appraised of this and we expect a more satisfactory RFG to be available in Thailand next month.

We do want to do some animal studies with the new RFG to make sure that the biological activity of the supplement is not lost to any major extent in cooking.

We felt that some of the methods for taking the anthropometric measurements needed improvement. For instance, the board used for obtaining reclining lengths had too much play in it and weights were being measured to the nearest 0.5 kilo rather than to 0.1.

We did not have a satisfactory method for recording and retrieving data. We have developed a clinical data sheet which we are having printed which will permit all data collected to be put on IBM cards. Arrangements have been made in Bangkok for the necessary card punching.

The possibility of developing a program for measuring the effect of nutrition programs on mental development in pre-school children in conjunction with Phase IV has been explored. We met with Dr. Chira Sritasuwan, the head of the Chiang Mai mental hospital, and found that he not only was interested

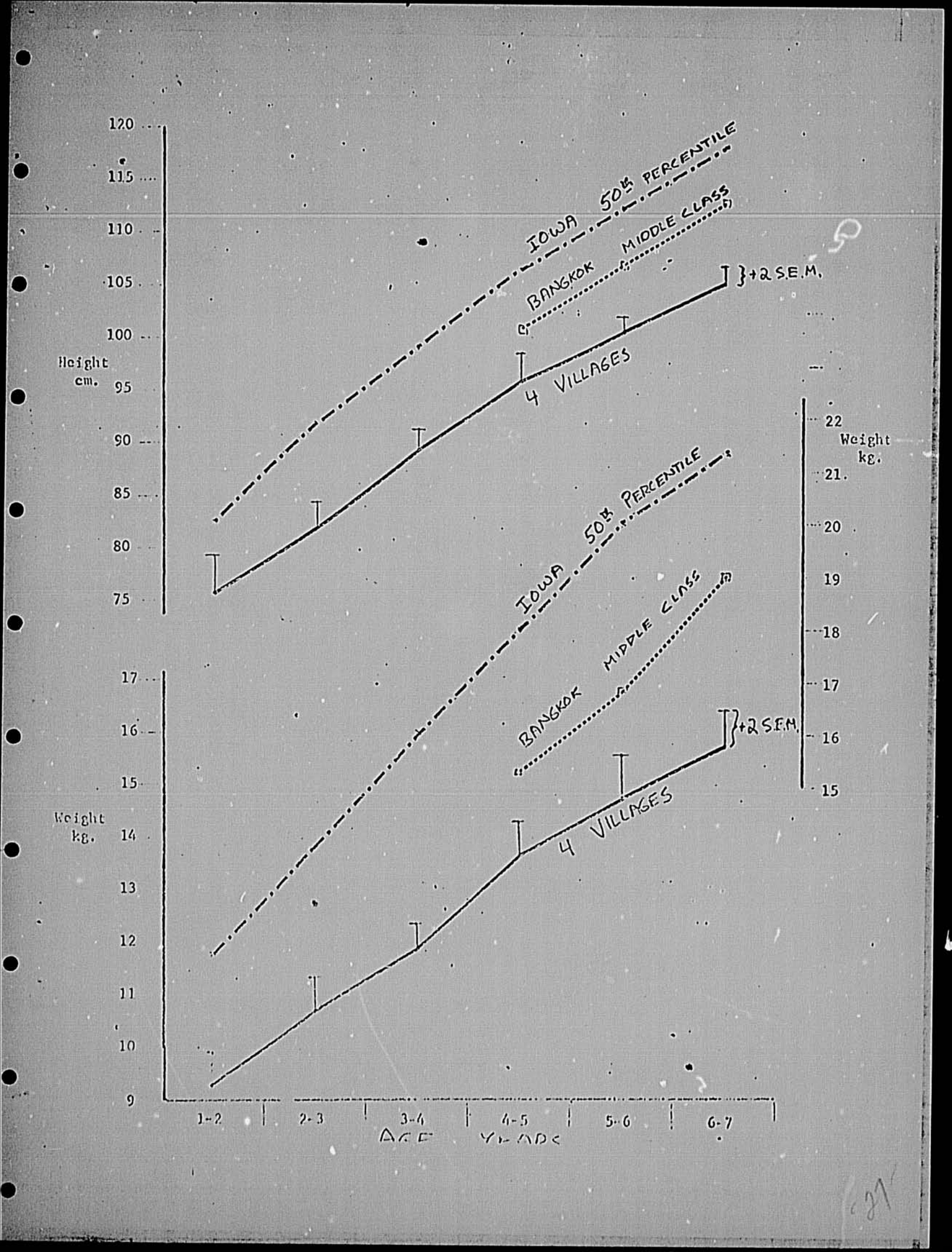
in such a study, but that last year he and his associates had done some testing of village children. We were all agreed that the first priorities in such a program should be the development of suitable methodology for use on rural Thai pre-schoolers.

Dr. Chira informed us that he had 4 psychologists on his staff who were interested in such a program and that last year a dozen medical students from the Chiang Mai medical school had approached him for programs for their elective time.

We believe that if funds are available we should arrange to send consultants from the United States to initiate a program with Dr. Chira. This summer, when Dr. Gershoff returns to Thailand, would be a good time to do this.

We feel strongly that in developing methodology for measuring mental development of Thai village children care should be taken not to upset the experimental objectives of Phase IV. The testing of methodology should be worked out in villages not included in Phase IV and at some later date the effects of the Phase IV program on mental development can be evaluated.

In writing of the Harvard-Thailand Rice Fortification Project, it should be pointed out that its success has been primarily due to the marvelous cooperation and ability of Dr. Amorn Nondasuta, director of the Division of Nutrition of the Thai Department of Health and his extremely able associate, Mr. Uthai Pisolyabutra. Their enthusiasm and interest in developing nutrition programs in Thailand has made Thailand an outstanding place to do collaborative research in nutrition.


Height cm.
120
115
110
105
100
95
90
85
80
75
IOWA 50th PERCENTILE
BANGKOK MIDDLE CLASS
+2 S.E.M.
4 VILLAGES
Weight kg.
17
16
15
14
13
12
11
10
9
22
21
20
19
18
17
16
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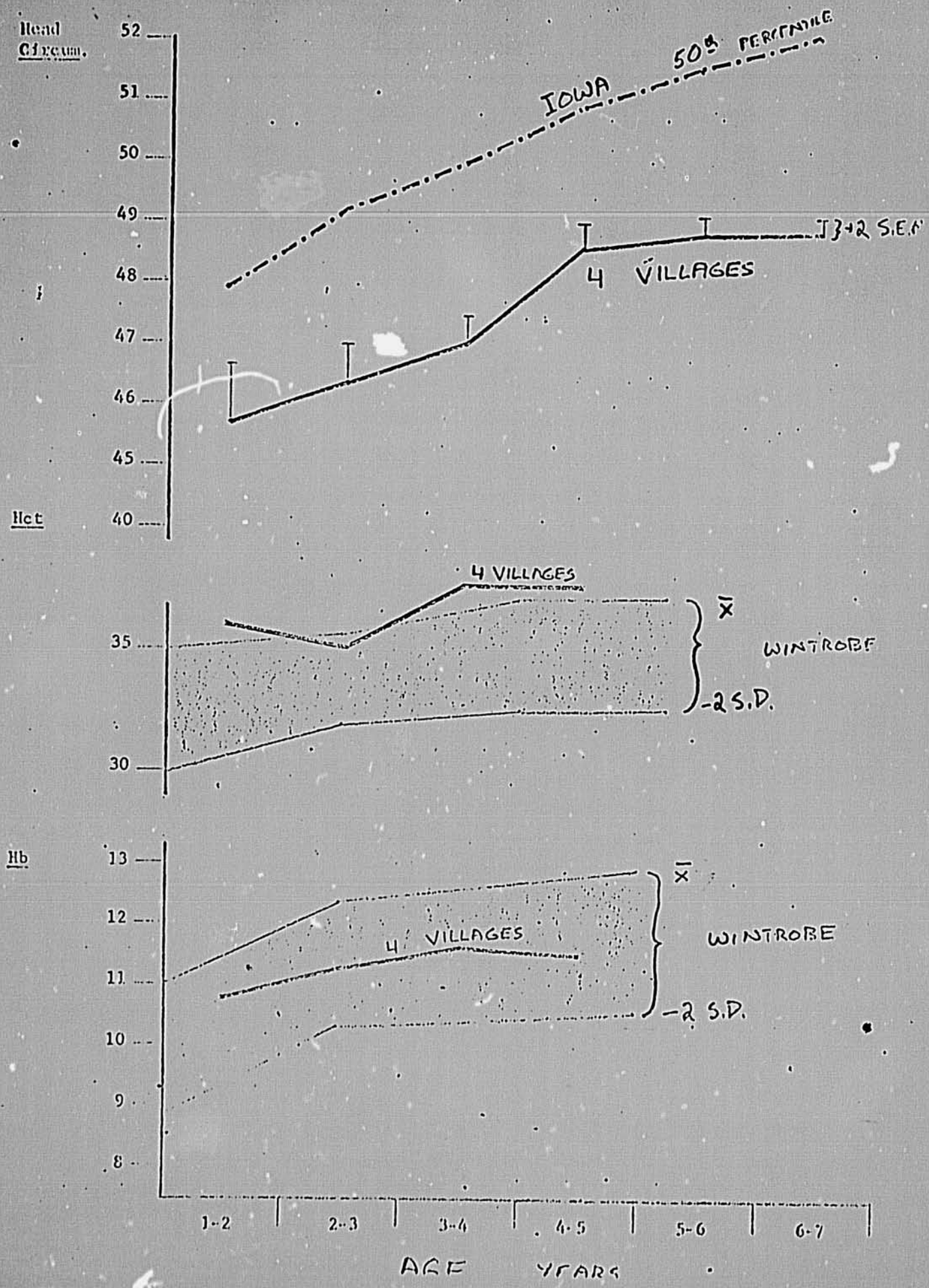
IOWA 50th PERCENTILE
BANGKOK MIDDLE CLASS
+2 S.E.M.
4 VILLAGES
1-2
2-3
3-4
4-5
5-6
6-7
AGE YEARS


Head Circum.
52
51
50
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48
47
46
45
IOWA
50th PERCENTILE
±2 S.E.M.
4 VILLAGES
Hct
40
4 VILLAGES
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$\bar{x}$
WINTROBE
-2 S.D.
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13
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4 VILLAGES
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WINTROBE
-2 S.D.
1-2
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5-6
6-7
AGE YEARS

28

Appendix 2

Progress Report - October 1970

Harvard-Thailand Rice Fortification Project

Contract No. AID/CSD-2170

In the latter part of August 1970 Dr. Stanley Gershoff went to Thailand to review the progress of Phase III of this contract, a pilot rice fortification field study and to make final preparations for initiating Phase IV, a full field study in early 1971. As previously reported the progress of the pilot study, the cooperation obtained from Thai Officials and village millers, the facilities available and the acceptance of the programs in the villages of Phase III receiving the rice fortification grains (RFG) have exceeded expectations and we are very pleased.

The children in the four pilot villages were re-examined in June and it appears that most of the problems of doing physical examinations have been solved.

Although Phase III has proceeded better than we expected, our experience has disclosed a few problems. First, there has been rising discontent in the raw control village. The village children have been examined twice but their parents see no sign of any benefits accruing to them. Furthermore, they have heard of health programs (not a part of Phase III) in other villages and they are not happy that they have received no aid.

We have had some problems in obtaining accurate skin fold measurements in squirming, pre-school children but we think that we have

minimized them. We are also still not completely satisfied with the RFG. We have now received 5 different batches of RFG from Ajinomoto. The initial shipments caked. The Ajinomoto Co. was appraised of this problem and they have evidently been experimenting with their RFG coatings. Lot 4 remained hard after cooking and was not satisfactory. However, lot 5 does not cake and is quite acceptable to the villagers.

We expect this Fall to study in rats the biological availability of the nutrients in RFG after cooking Thai style. The laboratory at the Thai Division of Nutrition has obtained amino acid analysis data on Thai rice with and without RFG before and after cooking. There is no doubt that the people in the villages have been using the RFG. Daily checks at the mills indicate that the RFG is being added to the rice. We have figures on the amount of rice milled in each mill every day and the amount of RFG used checks within a couple of percent of amount which should be added. Furthermore we have urinary thiamine excretion data, indicating that the RFG containing thiamine is being consumed.

It has been decided to initiate Phase IV, a full field study in January 1971 as scheduled. Twenty-five villages containing approximately 2600 pre-school children and a total population of about 15,000 people will be studied. Eighteen of these villages had been selected by early September of this year and the full cooperation of the millers and villagers been assured. Because of the difficulties observed in the raw control village of the pilot study some changes will be made in our experimental design. The design shall be as follows:

30

5 villages will receive day care centers and a placebo RFG

5 villages will receive day care centers and an RFG containing thiamin, vitamin A and Fe

5 villages will receive day care centers and the complete RFG containing lysine and theomine in addition to thiamin, vitamin A and Fe

5 villages will not receive day care centers but will receive the complete RFG.

5 villages will act as raw controls. In order to minimize the difficulties we have had with our raw control village, these villages will be selected in an area about 20 kilometers away from our other experimental villages or villages in which other major child health and/or nutrition programs have been initiated. The children in the raw control villages will receive the same initial and final physical examinations given in the other villages. However, the periodic examinations given in the raw control villages during the experimental period will be limited to weights and body lengths to avoid difficulty with the villagers. Ofcourse, if the experimental results obtained in the other 20 villages indicate that more complete physicals are needed in the raw control villages the option of expanding the periodic physical examinations will be available.

Concern continues to be expressed both in Boston and Bangkok about starting the full field study in January of 1971 with financial support assured only until June 1971. Nevertheless, we have felt that to drastically alter our time table at this time with Phase III proceeding smoothly would not be wise. It is expected that both Drs. Gershoff and McCandy will be in Thailand while the base line data for the full field

study are being obtained. It is only during part of the first three months of the year that they can arrange to absent themselves from their duties in Boston. The monsoons which occur in the summer in Thailand make it an undesirable time to start Phase IV.

To prepare for the start of Phase IV in January, 12 day care centers and 17 RFG dispensers will have to be built. Some additional personnel will have to be hired and additional transportation will have to be arranged.