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**PAN AMERICAN HEALTH  
ORGANIZATION**

**ADVISORY COMMITTEE  
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**A NUTRITION RESEARCH PROGRAM  
IN LATIN AMERICA**

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**PAN AMERICAN HEALTH ORGANIZATION**  
Pan American Sanitary Bureau, Regional Office of the  
**WORLD HEALTH ORGANIZATION**  
WASHINGTON, D.C.

## A NUTRITION RESEARCH PROGRAM IN

## LATIN AMERICA\*

Introduction. The Western Hemisphere contains a great land mass frequented by a rapidly increasing population. The land mass is underdeveloped from an agricultural and industrial point of view. The population, even at present, is poorly nourished. The vicious cycle of poor nutrition, low productivity, low standard of living, poorer nutrition, lower productivity, lower standard of living, etc., is not only continuing but in many areas increasing its tempo. A principal reason for this deteriorating situation, paradoxical as it may seem in view of modern science and technology, is the failure of economic growth to keep pace with marked increases in population. Population pressure, increasing as it is by virtue of modest advances in sanitation and in preventive and curative medicine leading to reduced mortality rates among infants, children and the elderly, has outstripped the performance of many Western Hemisphere nations in producing adequate supplies of food or generating sufficient foreign exchange to permit importation of minimal needed additional foods. The only presently feasible method of breaking the vicious cycle lies in altering environmental factors over which man can exercise control in such a way as to increase the ability of each nation to improve its nutrition and to do so with all possible speed.

Many measures toward this goal, such as those described above, are already underway. These represent, however, only a beginning, merely a fragment of the total measures needed if those areas of the hemisphere which are nutritionally underprivileged are to achieve their potential. The key lies in personnel. Without trained personnel, few advances are possible

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\*Prepared for the first meeting of the PAHO Advisory Committee on Medical Research by the Regional Advisor in Nutrition, PASB, assisted by Dr. N. S. Scrimshaw and Dr. D. M. Watkin, MIT, with the collaboration of Dr. J. B. Stanbury, Massachusetts General Hospital and Dr. J. Cravioto and Dr. G. Arroyave of INCAP.

The problem thereby resolves itself into a simple question: how can the requisite numbers of personnel be obtained? Obviously, one method is to generate new interest in better nutrition, new popular support for better nutrition, new economic resources for better nutrition. International and national government agencies, philanthropic organizations and corporate bodies are willing to invest in forward movement, not just maintenance of the status quo. Progress, development and advancement are virtually synonymous with research and its application. Research is, realistically, the basis for sound progress. It is certainly the means to the end of interesting and inspiring personnel to seek out careers in nutrition.

Research, however, does not suddenly condense out of a vacuum. Research must be first carefully oriented to fill most pressing needs. It must not be overly ambitious if it is to avoid the risk of failure. It must be adequately financed. It must receive direction and encouragement from qualified consultants. It must offer substantial opportunities to young individuals, not only for training but also for distinguishing themselves scientifically and for earning enough remuneration to provide decent livelihoods.

The present paper will present the main nutrition problems in the Americas and will give priorities to the research problems in nutrition.

The paper will be presented in the following outline form:

- A. The magnitude of the Problem
  - 1. Protein-Calorie malnutrition in infants and children
  - 2. Endemic goiter
  - 3. The Anemias
  - 4. Vitamin A deficiency
  - 5. Chronic malnutrition due to multiple factors

- B. Present Knowledge and Needs
- C. Priorities of Research Problems in Nutrition
- D. Summary of Priority Research Proposals in Nutrition

In the addendum to RES 1/6, supplementary notes are provided on the background to WHO/PASB activities in nutrition research.

### THE MAGNITUDE OF THE PROBLEM

The nutrition in the Americas embraces the antipodes of undernourishment and overeating. In the Americas, these two extremes are found in certain geographical areas and certain social classes, and have a history and economy of their own. For obvious reasons of priority, this document will deal exclusively with undernourishment, although this does not imply that overeating is not of importance as a public health problem. However, undernourishment is more serious precisely in those countries that have the fewest means with which to cope with it, whereas overeating is mainly a problem in countries whose need for international assistance is not urgent

### Specific Nutritional Problems

#### 1. Protein-calorie malnutrition in infants and young children

As is well known, the figures for mortality from deficiency diseases do not offer a trustworthy picture of nutrition problems. Apart from the fact that the registration of deaths is very incomplete in many countries, undernourishment is rarely the final cause of death.

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Children suffering from kwashiorkor -- severe protein deficiency--or from marasmus die mainly of bronchopneumonia, diarrhea, or other infectious diseases and these are entered on the death certificate as the cause of death. Thus, if the order of priority of health programs is established solely on the basis of mortality rates, serious errors of interpretation may occur. Nevertheless, even with these reservations, it is an impressive fact that for every child in the age group 1-4 who dies of malnourishment in the United States of America, 300 are recorded as dying of this cause in some countries of Latin America, a small proportion of the total for whose deaths malnutrition is directly or indirectly responsible. Death per 100,000 in the age group 1-4 recorded as due to malnutrition in 1959-60 were for the United States of America, 0.4; El Salvador, 143.4; Colombia, 124.7; Mexico, 124; Guatemala, 78.3; and Venezuela 63.2.

As has been mentioned above, the death rates attributed to malnutrition or kwashiorkor do not represent the total death rate from these causes. This point is illustrated by a study carried out by INCAP in four villages of Guatemala. Each death was individually investigated and the cause determined through investigation and compared with that given in the Civil Register. The results of 222 cases showed that nearly 40% of those in the 1-4 age group died with edema, skin lesions, hair changes, apathy and the other signs of acute kwashiorkor. Of the remainder nearly all died in the course of relatively brief episodes of either diarrhea of infectious origin or complications of common childhood infections, none of which would have been fatal to any significant number of well-nourished children. The conclusion is that improved nutrition would not only eliminate the nearly 40% of all deaths caused by kwashiorkor, but also markedly decrease the number of deaths apparently due primarily to infection.

The synergism between infection and malnutrition is a major reason why total mortality from all causes in children between the ages of 1 and 4 years in Latin America is 20 to 30 times higher than in the United States of America. Were the mortality rate in children in the age group 1 to 4 the same in Latin America as it is in the United States of America, almost 300,000 fewer children in that age group would die every year.

Moreover, the excessive morbidity and retardation of both physical and psychomotor development would be corrected for hundreds of thousands of additional children.

## 2. Endemic Goiter

Another serious nutritional problem in the Americas is endemic goiter. Endemic goiter is considered to be a public health problem when its prevalence is greater than 10%. In the American Continent there are areas in all countries in which the prevalence is higher than 10%. Uruguay, where the problem was thought not to exist, is no exception.

In Argentina the prevalence in some provinces is between 70 and 80%. In Bolivia there are extensive areas where the prevalence is 40% and some where it is between 50 and 60%. In Brazil, in the State of Minas Gerais, the prevalence is 44%; in the southeast it is 27%; in the middle east, 53% and in the south, 27.7%. In Chile, in the province of Santiago the average prevalence in school children is 11%, but it is much higher in some of the valleys in the foothills of the high mountains. In Colombia the prevalence is extremely high, reaching 89% in Cauca, 81% in Caldas, 67% in Boyacá, 75% in Santander del Sur, and 71% in Valle; one survey covering the whole country showed an average prevalence of 53%. In Costa Rica the prevalence ranges from 10 to 26%; in Ecuador it is 50.5%; in El Salvador, 30%; in Guatemala, 30.5%-- the highest in Central America; in Honduras, 22%; in Mexico, 19%; in Nicaragua, 26.5%; in Panama, 31.5%; in Paraguay, 30%; and in Peru the prevalence in males is 36% and in females 64%, and in certain areas, such as the province

of Rodriguez de Mendoza, it is 100%. In Uruguay it ranges from 6 to 17%, and in Venezuela, in the Andes, from 10 to 89%.

### 3. Anemias

A third specific nutritional problem in most of the Latin American countries is that of the iron-deficiency anemias. Although no accurate figures of their prevalence are available, preliminary estimates indicate that it is extremely high in some areas.

The general view held in the past, namely, that the fundamental cause of these anemias was infestation with parasites, especially encylostoma, is at present being revised and, while the importance of that factor is not discounted, it is clear that others, such as the low iron intake in children, the loss of iron by sweating in the tropics, and poor absorption of iron, may play an important role in the genesis of these anemias. This problem is at present one of the most interesting aspects of public health research.

Table I shows recorded death rates from anemias in different countries of Latin America. Many of the countries report rates from 10 to 30 per 100,000 population, which may be considered very high as compared with the U.S.A., Canada, and other countries where the rate is around 2 per 100,000. For the three regions, in 1957, the rates per 100,000 population were 1.8 in Northern America, 12.4 in Middle America and 7.4 in South America. (Table II)

Table III shows the death rates attributed to anemias by age groups in three countries. It is clear that these deaths are concentrated both in early life and in the later adult life.

More interesting, perhaps, are the figures on morbidity, although very few studies have been made of the prevalence of these anemias in Latin America. In Iquitos (Peru) 50% of school children show hemoglobin levels below 10 gm. per 100 cc. (Gandra). In Esmeraldas (Ecuador) 13.5% of the persons examined

show hemoglobin levels below 10 gm. (ICNND). It is believed that iron deficiency anemias are widespread in nearly all of the countries of Latin America.

TABLE I

Death Rates from Anemias per 100,000 Population in the Americas  
1950-1959

Country	1950	1951	1952	1953	1954	1955	1956	1957	1958	1959
Northern America										
Canada	3.6	3.2	2.8	2.6	2.1	2.1	2.2	2.0	2.3	1.9
United States	2.7	2.6	2.6	2.3	2.0	1.9	1.9	1.8	1.8	2.0
Middle America										
Costa Rica	31.2	28.4	16.2	17.2	19.0	16.6	15.5	13.9	12.0	9.5
Dominican Republic	11.5	14.3	13.0	13.4	14.2	12.5	14.4	15.2	12.2	...
El Salvador	10.3	11.9	12.5	9.8	9.9	10.0	12.5	10.9	12.9	13.0
Guatemala	24.1	25.6	27.6	25.4	24.3	28.1	36.0	34.0	32.9	35.3
Honduras	...	...	...	10.2	...	10.5	9.6	9.4	9.2	11.1
Mexico	9.5	9.9	10.2	11.2	9.1	10.3	10.2	10.0	...	...
Nicaragua	7.1	...	...	...	7.8	11.7	9.2	9.8	11.1	10.5
Panama	7.3	...	11.2	11.0	9.2	16.7	19.5	15.2	12.5	14.8
South America										
Argentina	...	...	...	1.3	1.9	1.9	1.7	...	...	...
Bolivia	32.8	30.9	35.7	41.9	9.2	...	...	...	...	...
Chile	3.6	2.9	2.8	3.0	2.6	2.3	1.6	2.0	1.6	1.2
Colombia	...	...	...	14.8	19.8	20.2	19.9	20.5	19.1	17.1
Ecuador	...	...	...	...	20.5	20.2	22.6	22.7	24.6	...
Paraguay	4.4	4.9	...	4.2	3.2	2.7	3.4	3.0	4.7	...
Peru	6.9	7.8	8.3	7.9	2.6	...	...	2.7	3.4	...
Uruguay	...	1.7	2.5	2.0	2.4	2.4	...	...	...	...
Venezuela	3.5	3.5	2.8	3.3	2.6	2.8	3.0	2.9	2.8	2.4

Sources: WHO, Annual Epidemiological and Vital Statistics Report  
UN, Statistical Office



TABLE II

Death from Anemias with Rates per 100,000 Population in Three Regions of the Americas, 1957\*

Region	Anemias (290-293)	
	Deaths	Rate per 100,000
Northern America	3,315	1.8
Middle America (a)	5,573	12.4
South America (a)	4,571	7.4

(a) Includes eight countries in Middle America and seven in South America

\* When not available for 1957, data for most recent year available were used

Sources: WHO, Annual Epidemiological and Vital Statistics Reports  
UN, Statistical Office

TABLE III

Number of Deaths from Anemias with Rates per 100,000 Population by Age in Colombia, United States and Venezuela, 1956-1958, Average

Age Group	Number			Rate per 100,000		
	Colombia	United States	Venezuela	Colombia	United States	Venezuela
All ages	2,622	3,108	177	19.8	1.8	2.9
Under 1 yr.	140	135	15	29.7	3.6	6.9
1-4 years	471	167	36	28.1	1.1	4.5
5-14 years	375	142	24	11.3	0.4	1.6
15-44 years	694	326	50	12.3	0.5	1.8
45-64 years	483	512	25	35.5	1.5	3.7
65-74 years	217	699	13	83.3	7.2	12.1
75 and over	299	1,124	14	162.2	22.5	24.6
Not stated	13	3	0	...	...	...

Sources: Colombia, Anuario General de Estadística, 1956, 1957, 1958.  
U.S., Vital Statistics of the United States, 1956, 1957, 1958.  
Venezuela, Anuario de Epidemiología y Estadística Vital, 1956,  
1957, 1958.

#### 4. Vitamin A Deficiency

Apparently vitamin A deficiency is a nutrition problem in Latin America of greater importance than originally anticipated. Dietary surveys made in Central America, Ecuador, and Peru have shown very low intakes of vitamin A. Although severe cases of keratomalacia or xerophthalmia are not frequently found, milder manifestations, such as night blindness, are relatively common in some areas. Biochemical findings indicate that this problem exists in Ecuador, Central America and other countries, among lower income groups. It is significant that Bitot's spots were found in one per cent of the civilian population in Ecuador, although it is recognized that not all cases can be attributed to vitamin A deficiency.

#### 5. Chronic Malnutrition Due to Multiple Factors

As in the past, in some parts of the world today malnutrition takes the form of acute and easily recognized nutritional diseases of the classic type. At the present time in Latin America it is more likely to occur as a combination of borderline deficiencies of several nutritional factors including calories, protein, vitamin A, riboflavin, iron and iodine. Young children may show few physical signs of deficiency yet be retarded in their growth and psychomotor development, be more susceptible in infection and experience a high morbidity as well as mortality. Similarly, adults are small, frequently sick, listless and unable to realize their full physical and mental potential

Other major nutrition problems of the Americas are also discussed in the report of the Nutrition Advisory Group in National Health Planning but are not the subject of proposed specific recommendations at this time.

PRESENT KNOWLEDGE AND NEEDS

Available information will produce paper solutions for a high percentage of specific nutritional disease problems in the Americas. In the field of protein, iodine, iron, vitamin A and riboflavin deficiencies, ample knowledge of the prevalence of the deficiencies and of the practical methods for alleviating the deficiencies is available. Translation of the paper solution into reality is a task so formidable that present personnel are incapable of achieving more than localized success. Greater public interest in the translation, more resources and most of all more personnel at all levels are required. Research, as noted above, provides one means of generating interest, resources and personnel.

Present knowledge does not, however, provide answers for numerous questions of less immediate, practical significance but which nonetheless represent important scientific gaps in the total picture of deficiency diseases. As carefully documented in RES 1/6, ANNEX I, the relation of genetic constitution to the prevalence of goiter is a segment of the total goiter problem in need of analysis. As noted in RES 1/6, ANNEX II, the contribution made by protein deficiency to the total picture of iron deficiency anemia is not at all established by existing data. As indicated in RES 1/6, ANNEX III, there is only rudimentary information on the relationship between mental development and malnutrition.

The interrelation of nutrition to infection has received considerable attention from Central American workers in the past five years. Nonetheless, the variations in infective agents, in environmental and climatic factors and in economic conditions, as well as variations in

traditional dietary patterns, would alone suggest the need for investigations in other areas. When the difficulties and long duration of such investigations are considered, it is apparent that strides in understanding these complex interrelations will not come rapidly.

Present knowledge, therefore, would permit solution of a high percentage of high priority nutrition problems in the Americas but only provided sufficient numbers of trained personnel were available at all professional levels. It would in no sense, however, provide information to fill innumerable gaps in scientific knowledge presently apparent to experts in their respective fields. Consequently, research in selected problem areas satisfies the dual needs of providing more trained personnel and fulfilling requirements for more knowledge.

#### PRIORITY OF RESEARCH PROBLEMS IN NUTRITION

Priority for research must be determined not only on the basis of need but also on the readiness of a given program for implementation. With due attention to both these considerations, the Research Planning Office, the Regional Adviser in Nutrition and the Special Consultants, guided by the recommendations of the WHO Consultants, the WHO Scientific Group and the PAHO Nutrition Advisory Group, recommend that research be directed first into the following areas.

- 1) Endemic goiter (iodine metabolism);
- 2) Anemias (iron, protein and vitamin metabolism);
- 3) Effects of nutrition on patterns of growth and psychomotor

development of children;

4) Nutrition and infection.

Needs for research in vitamin A deficiency is acknowledged but not given priority on the PAHO program only because of WHO proposed activity in the Americas in this field. Acknowledged also is the need for further research in the testing of protein-rich foods. This is not given priority because of the active programs now under way under the general direction of the WHO/FAO/UNICEF Protein Advisory Group. Studies in problems of riboflavin deficiency, lactation and mortality due to malnutrition in infancy and childhood will be prepared at a later date.

SUMMARY OF PRIORITY RESEARCH

PROPOSALS IN NUTRITION

A detailed report on the endemic goiter research proposal is contained in RES 1/6, ANNEX I. This report, prepared by Dr. John B. Stanbury, discusses the background, present status and future development of work in endemic goiter and iodine metabolism in five centers already known through their personnel and facilities to be capable of expanding rapidly research in this general field. To this aim, Dr. Stanbury made a field trip in April, 1962 to several countries of Latin America, as consultant to PASB, to ascertain the possibilities of a combined research program on endemic goiter.

Two detailed proposals for research in anemia are contained in RES 1/6, ANNEX II. The first, representing a project which is under consideration for NIH support, is a careful study by modern methods of the pathogenesis of anemia in Trinidad, prepared by Dr. Chopra in collaboration with Dr. Watkin. Since a large-scale ICNND-sponsored Survey of Trinidad and other Eastern Caribbean Islands has already established prevalence rates of anemia

in randomly sampled populations, the specific aim of this project is to concentrate on unknown areas in pathogenesis, such as the role protein deficiency may play in so called iron deficiency anemia. The second, representing a completed proposal, suggests a survey of hematologic values in lactating women, pre-school children, school children and selected adult groups in Central America and Panama. Since no survey comparable to that performed under ICMND sponsorship in the Eastern Caribbean has been performed in Central America, there is no adequate knowledge at present of the true prevalence of anemia. The Institute of Nutrition of Central America and Panama, while fully aware of the importance of the anemia problem, has not yet found financial support to undertake a systematic study of anemia.

Research project proposals are included in RES 1/6, ANNEX III, describing in detail proposed studies on the effect of nutrition on the patterns of growth and development and on the influence of nutritional status on mental development, prepared by the Staff of INCAP. Both proposals are aimed specifically at relating physical and psychological development to the nutritional status of the child. Differences in such important variables as ethnic background, social status, family size, parental education and general health must receive consideration pari passu with that given nutritional status. Preliminary work carried out with painstaking care for over five years in Mexico can leave little doubt that malnutrition during infancy and early childhood may be reflected in preventable damage to the minds of children who might, with better nutrition, increase their ability to absorb education and thereby contribute more to the progress of their countries.

Proposals for expansion of existing and inauguration of new programs in the study of the interrelations of nutrition and infection are

presented in RES 1/6, ANNEX IV, prepared by Dr. N. S. Scrimshaw. As noted above, the complexities of the interrelationships in this area require the reinforcement of the Central American program and the development of complementary programs in other geographic areas.

BACKGROUND INFORMATION ON WHO/PASE  
ACTIVITIES IN NUTRITION RESEARCH

PAHO is already directly involved in research activities through the Institute of Nutrition of Central America and Panama (INCAP) in Guatemala City, through its Adviser in Nutrition to the Eastern Caribbean assigned to the Caribbean Nutrition Center (CNC) in Trinidad, through its Adviser in Nutrition assigned to the National Institute of Nutrition (INNE) in Ecuador, through its collaboration with the government of Peru in a study of anemia and through its participation in some of the nutrition surveys in this Region carried out by the Interdepartmental Committee on Nutrition for National Defense (ICNND) of the United States of America.

In Trinidad and Tobago, the educational aspects of these programs were complemented by appropriation of funds for equipment to increase the research potential of the Caribbean Nutrition Center in its search for new sources of protein foods. The Nutrition Education and Training Programs are influential in creating public demand for more research leading to better nutrition. Coordination of PAHO activities in the field of nutrition is assured by frequent communications between Washington and Geneva and especially by the fact that numerous consultants serve on both WHO and PAHO. Coordination has also been established with FAO and UNICEF.

In February, 1960, a group of consultants from WHO gathered in Geneva to outline research needs in nutrition. The report of this meeting, later reviewed by a Scientific Group in New York during March, 1960, contained 127 different specific suggestions for needed nutrition research.



From these suggestions WHO sponsored research programs in the Western Hemisphere have been drawn. One of these, a study of iron deficiency anemia, is being conducted in Venezuela (Iron Deficiency Anemia and Hookworm Infection) Venezuelan Institute of Scientific Investigations, Dr. Marcel Roche, Director, Caracas. This study is part of a world-wide WHO sponsored study of anemias, other segments of which are being conducted in India, South Africa and Mauritius. WHO has recently received a grant from the National Institutes of Health of the United States of America for surveys throughout the world, including the Western Hemisphere, of the prevalence of xerophthalmia and keratomalacia due to vitamin A deficiency. WHO has already communicated with PAHO about recruiting a suitable consultant to plan a program for this hemisphere. PAHO is represented on the WHO/FAO/UNICEF Protein Advisory Group and through the Institute of Nutrition of Central America and Panama has sponsored successful investigative and developmental work on protein-rich foods.

NUTRITION IN NATIONAL HEALTH PLANNING:

From January 10 to 13, 1962, a meeting (called by the Director) of the PAHO Nutrition Advisory Group was held in Washington. The Group was asked to recommend both immediate and long-term measures within the framework of national health planning, for application to the field of nutrition in the Western Hemisphere. Impetus for the meeting call came from consideration of provisions of the Act of Bogota and the Punta del Este Charter of the Alliance for Progress. Paragraph 1-DIH of the Act of Bogata calls for "the strengthening of programs of nutrition for low income groups." Among the goals of the "Ten Year Public Health Program" (Resolution A.2) of the Punta del Este Charter were: 1) "to make substantial improvements in the

feeding and nutrition of the most vulnerable sectors of the community by increasing of animal or vegetable proteins"; and 2) "to reduce the rate of mortality in children under five years of age to one-half its present rate, during the present decade."

Believing firmly that achievement of such goals requires the formulation of nutrition programs as part of national health plans, which in turn must necessarily be incorporated into economic and social development measures, the Director requested from the Nutrition Advisory Group a well balanced, realistic, scientifically and economically sound report outlining the directions of future development and the priorities to be established in implementing recommendations.

The Group reported from its deliberations that, as far as prevalence and harmful effects on populations are concerned, the most important nutritional deficiencies are: 1) protein deficiency, quantitative and qualitative; 2) iodine deficiency; 3) iron deficiency; 4) vitamin A deficiency; and 5) riboflavin deficiency. The Group also noted the significant interrelations between malnutrition and infection in adversely affecting health in general, nutritional status, working capacity, mortality rates among infants and small children and morbidity rates among older children and adults. It identified the need for clarifying the role nutrition plays in physical and mental development of infants and children. The group acknowledged the importance of economic factors and social customs, traditions and taboos in influencing nutritional patterns.

In recognizing the need for additional research in the field of nutrition in the Western Hemisphere, the PAHO Nutrition Advisory Groups noted the necessity of determining and re-evaluating at appropriate intervals the distribution and severity of protein-calorie malnutrition, endemic goiter,

nutritional anemias, hypovitaminosis A and riboflavin deficiency. The Group specifically recommended clarification of the role nutrition plays in physical and psychomotor development. The Group also urged continuation of existing programs in the development of protein rich foods, in the interrelationships of nutrition and infection and in the effects of malnutrition on capacity for lactation, physical labor and adaptation to nonnutritional environmental factors.

The Advisory Group, while noting the document prepared for world-wide use by WHO Consultants in 1960 (v.s.), recommended as priority items the proposals mentioned in RES 1/6 and advised that PAHO assume an active role in stimulating and, where possible, supporting those proposals.

III (a) Rio de Janeiro

The Institute of Biophysics in Rio de Janeiro is beautifully equipped for the most advanced and elegant studies of radiobiology. Dr. Luis Carlos Lobo is in charge of thyroid research at this Institute where he spends most of his time. He is also in charge of the Radioisotope Unit at the Hospital. His recent studies have included a survey of patients with endemic goiter in the state of Goiaz for the relationship between goiter and antithyroglobulin antibodies. No relationship was found. He has also studied the relationship between endemic goiter, cretinism and Chagas' disease, the last being ascertained by a complement fixation test. Again, no relationship was found and this perplexing old problem seems to have been solved. It should be said that Lobo is obviously an extremely well trained scientist, entirely capable to do first class investigation. He is competent in chromatography, and such other scientific techniques as are required for problems relating to endemic goiter and cretinism.

With Dr. Lobo and his colleague, Dr. Pompeu, a neurologist from the University Hospital I visited Goiaz, an area of endemic goiter and cretinism in the state of Goiaz, approximately 1200 kilometers west and north of Rio. Of particular interest was to survey a large group of cretins at the Azuylo de St. Vicenti do Paulo. Most of these cretins conform to the classic Swiss description. Most were deaf. All were of short stature. All had oligophrenia, and interestingly, Dr. Pompeu found that all had distinct spastic neurological changes.

Dr. Lobo and his group are in a particularly advantageous position to investigate in depth the problem of cretinism. He is interested in bring-

ing a series of these cretins from Goiaz to Rio for study. His studies will include detailed neurological assessment, including electro- and pneumoencephalography, examination of the spinal fluid, electromyography, audiometry, and complete x-ray study of the bony skelton. In the course of this detailed thyroid investigation will be made, and possibly biochemical studies of thyroids in suchcases where it seems expedient to have the thyroid biopsied. It seems clear that Dr. Lobo is equipped both intellectually and with apparatus and some supporting funds to pursue his studies.

IV. Caracas

Endemic Goiter Project

Justification for budgetary items for support of research  
on endemic goiter in Venezuela

- (1) It is important to develop adequate field equipment. The instruments would have to be specially prepared for use under conditions of high humidity in the tropics. This problem has to be given high priority.
- (2) Obtaining additional fixed laboratory equipment and more refined equipment for chromatographic studies. There is particular interest in using C<sup>14</sup>-labeled compounds (triiodothyronine and thyroxine) and possibly doubly tagging these compounds with both I<sup>131</sup> and C<sup>14</sup>.
- (3) Expeditions. It would be helpful to obtain in the future a sum for such expeditions (with the exception of the plane transportation which is covered by the Air Force.
- (4) The purchase of isotopes.

1. <u>Field Equipment</u>	<u>Bs</u>	<u>U.S. \$</u>
a) Development of one transistorized scaler		
Material Bs. 1,500.		
Manpower " <u>3,500</u>	5,000.	_____
b) Manufacture of a second, similar scaler		
Material Bs 1,500.		
Manpower " <u>600</u>	2,100.	_____
c) 2 DS1-A Scintillation Detectors (Nuclear-Chicago)		2,000.

	<u>Bs</u>	<u>U.S. \$</u>
d) Electrical plant	2,000.	
e) Batteries and battery charger	200.	
f) Centrifuge	_____	65.
g) Short-wave field radio transmitter	1,500.	_____
2. <u>Additional Laboratory Equipment</u>		
a) 4-pi-Radiochromatogram Scanner (Atomic Accessories, Inc.)		
RSC-160 4-pi-Scanner US\$	1,815.	
Recorder PWS-T-62-100 N	1,720.	
Ratemeter BA-432A	625.	
Recorder paper, FGG-	<u>100.</u>	
Geiger Gas, etc.		4,260.
b) DS-303 Well Scintillation Detector		3,205.
c) Analyzer-Computer 132A		2,000.
3. Additional costs of two expeditions per year	6,000.	_____
4. <u>Isotopes and labelled compounds:</u>		
I <sup>131</sup>		1,000.
C <sup>14</sup>		1,200.
	Bs 16,800.	\$13,730.
Grand Total (One US\$=Bs 4,50)	US	\$17,463.

RECOMMENDATIONS FOR RESEARCH PROJECTS IN ANEMIAS  
IN LATIN AMERICA

As mentioned in the body of the report (RES 1/6), the Headquarters Office of WHO has sponsored world-wide research programs in nutrition. Among the areas receiving special attention are the anemias, one such study being carried out in the Western Hemisphere by the Venezuelan Institute of Scientific Investigations of which Dr. Marcel Roche is Director. The research programs suggested in this paper complement the WHO activities being carried out in this hemisphere.

Information Required.- Throughout the Americas the amount of anemia and its several associations with malnutrition, parasitism and infectious disease are generally underestimated and little understood. Nutrition surveys sponsored by ICNND in Ecuador, Peru, Colombia, Chile, the West Indies and Uruguay have provided extensive information on the prevalence of anemia by area and among various population groups. The same surveys have provided limited information on the morphology of the peripheral red cells in such anemias. The stage is set, therefore, for a more intensive assault on the pathogenesis of anemias in the Americas. Understanding the pathogenesis of particular anemias is an essential prerequisite to the introduction of measures for anemia prevention and control. Three major types of anemia are present in the Americas: 1) hypochromic, microcytic; 2) macrocytic and 3) hereditary. Probable pathogenetic factors



in type (1) are: a) deficiency of dietary iron; b) excessive loss of iron via skin and bowel; c) parasitism and possibly d) protein deficiency. Probable pathogenetic factors in type (2) are: a) folic acid deficiency; b) B<sub>12</sub> deficiency and possibly c) deficiency of ascorbic acid. Probable pathogenetic factors in type (3) are the genetic variants in individuals manifesting sickle cell and Mediterranean anemia. Since it is essential that limited resources be concentrated on specific causal factors of major importance, a precise analysis of pathogenesis must be the first step toward reducing the prevalence of anemias.

Therapeusis will suggest itself naturally when pathogenesis has been determined in specific cases. In the Americas therapy must not only assist the individual but must be practical for application to population groups. In consequence, far more is involved than applying a textbook solution to an identified problem. Food supply, dietary custom, environment, economics and hereditary and multiracial backgrounds suggest that practical solutions must be novel and thoroughly investigated in man prior to their introduction as public health measures. Therefore, the second step in reducing the prevalence of anemia must include not only therapeutic trial but also the trial of new, practical and acceptable variations on basic therapeusis.

RESTRICTED

## I. TRINIDAD

Anemia has received top priority among problems being attacked by the Caribbean Nutrition Center and the Nutrition Program of the Government of Trinidad and Tobago. The long-term goal of this research is to reduce the high prevalence of anemia among the population of Trinidad.\*

Specific Aims: The specific aims of the project are

- 1) to identify the major environmental (including nutritional) and hereditary factors and to quantify the relative importance of these factors in the pathogenesis of anemia in Trinidad;
- 2) to investigate therapeutic measures suggested by (1) with the objectives of (a) confirming by therapeutic trial the pathogenetic role of the environmental or hereditary factors and (b) seeking practical measures leading to a reduction in the prevalence of anemia.

Data collected during an ICNND-sponsored nutrition survey in August 1961, as well as the clinical records of practicing physicians, pediatricians and hematologists marked anemia as a major health problem in Trinidad. Despite recognition of the problem, little has been done in a systematic way to identify and quantify as to relative importance various

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\* This project has been submitted by the Director, PASB, to the National Institutes of Health where it is now under consideration. The recommended extension of this project appears below on page 10.

- 4 -

pathogenetic factors. Since the pathogenesis has not been worked out and its components quantified, control measures have lacked specificity and limited resources have been ineffectual because of the diffusion of approach.

Method of Procedure: Data are available from the ICNND-sponsored nutrition survey indicating the nutritional status of 4,302 individuals selected at random from a detailed statistical frame. Laboratory evaluations, including hemoglobin concentrations, hematocrits and examinations of feces for parasites were performed on 536 of the individuals examined, the subsample also having been selected by a random procedure. Dietary intake was estimated in families representing 1,725 individuals by the 24-hour recall method and in twenty-one families by actual weighing of foods eaten and chemical analyses of the nutrient content of aliquots of those foods. These data established the percentage of the population with anemia, the distribution of anemia by age, sex and race and the distribution of anemia by geographic location. They also provide information on the nutritional status of individuals with respect to protein, riboflavin, thiamin, ascorbic acid, vitamin A and carotene. In addition, they quantify the dietary with respect to such nutrients as iron, protein, folic acid, vitamin B<sub>12</sub>, iodine, copper and cobalt, among others.

The availability of these data have justified moving directly to the identification of factors involved in pathogenesis.

This will be accomplished by: a) application to anemic individuals identified in the above mentioned survey of additional diagnostic procedures such as complete red blood cell indices, morphologic evaluation of peripheral blood smears, reticulocyte counts, histologic examination of bone marrow biopsies, hemoglobin electrophoresis, plasma vitamin B<sub>12</sub> concentrations, concentrations of folic acid and its metabolites in blood and urine and the quantification of parasites in blood, urine and feces; b) diagnosis and estimation of the severity of coexisting bacterial and viral infections; c) serial measurements during the consecutive application of nutritional and medicinal therapeutic maneuvers to provide confirmation of pathogenesis and d) variation in the order in which nutritional and medicinal therapeutic measures are applied, since it is anticipated that the anemias studied may have different or multiple pathogeneses.

Of particular interest in this study will be the opportunity to assess the role of protein deficiency, observed during the dietary evaluation aspects of the survey, in the pathogenesis of anemias in Trinidad. In addition, the role of protein deficiency in aggravating the anemias produced by iron deficiency or by parasites or by combinations of the two will be evaluated.

Significance of this Research: Anemia is a major health problem in Trinidad, not to mention its dependent island Tobago and other Eastern Caribbean islands also covered in the 1961

ICNND-sponsored survey. Research on similar problems in technically advanced countries provides certain guide lines for further investigation but does not provide answers to the questions of etiology, pathogenesis, secondary consequences, therapy or prevention of anemias such as are found in Trinidad. Information concerning these anemias is not available from investigations of a comprehensive nature using modern methodology. Consequently, opinions in Trinidad with respect to etiology, pathogenesis, complications, treatment and prevention of anemias are manifold, and, therefore, control measures by both private and public sectors of medicine diffuse and sporadic.

In large measure the significance of this research lies in its unique chance to delve immediately into problems which have already been specifically delineated by a scientific survey, its ability to apply advanced diagnostic methodology directly to specific individuals identified by the survey and its opportunity to unravel the tangled skein of theory on the pathogenesis of anemia in the Caribbean. Furthermore, this research affords an unparalleled opportunity for investigation of theoretical postulates such as the role of protein deficiency in the genesis of anemias. Findings of this investigation will have application to problems in the pathogenesis of anemias not only within but also outside of the technically underdeveloped world. Most of all, it takes advantage of a unique set of circumstances enabling it to focus a combination of personnel,

facilities, administration, scientific know-how and modern instrumentation on a well defined, circumscribed problem in a sharply delineated area. It, therefore, serves as an ideal pilot plant for forthcoming campaigns to eradicate anemia from the Hemisphere.

Personnel and Facilities Available: The methodology proposed for these studies is well standardized for technically developed countries in temperate zones. It will of necessity have to be modified to meet climatic conditions in Trinidad; however, since all facilities required for such modification are locally available and since experienced personnel and consultants are available to assist in these modifications, no difficulty is anticipated in altering the procedures to meet existing conditions and climate.

1. Personnel

- a. Joginder E. Chopra, M.D., M.P.H., M.S. (Nutrition) Adviser in Nutrition, Eastern Caribbean, PAHO.
- b. Barbara Birchwood, M.D., Internist, Maternal and Child Health.
- c. D.B.E. Quamina, M.B., B.Ch., D.P.H., Internist, Public Health.
- d. John D. Arneaud, M.B., B.S., M.R.C.R., (Eng.), L.R.C.P. (London), pathologist and hematologist.
- e. Lancelot Massiah, M.B., B.Ch., Pathologist and hematologist.
- f. Merwin Henry, M.B., B.Ch., Pathologist and hematologist.
- g. Bruce E.R. Symonds, M.B., B.S., M.R.C.P. (Lond.) Pediatrician.

h. Milton F. McDowall, L.M.S., P.M.Bd., Pediatrician.

2.- Facilities: The Government of Trinidad and Tobago has provided a large building for a Nutrition Center and, in addition, a Metabolic Study Unit permitting investigations in up to ten subjects. A well equipped analytical biochemistry laboratory was left in Trinidad at the end of the ICNND Survey and has been put into operation at the Nutrition Center under the direction of the PAHO Adviser in Nutrition and Consultants in collaboration with Trinidad personnel. A so-called Expanded Nutrition Program in the amount of \$75,000 ( USA ) with appropriate matching funds from the Government of Trinidad and Tobago has been inaugurated under the joint sponsorship of the government, UNICEF, FAO and PAHO. Under the terms of this program, laboratory equipment in the amount of \$6,000 (USA) plus shipping charges will be used to complement existing laboratory apparatus, particularly to provide the means of performing food analyses. The nutrition Center library is gradually accumulating basic texts, periodicals and other reference materials.

Budget of Present Program:

1) <u>Personnel</u> :	<u>\$12,900</u>
Biochemist	7,000
Hematology Technician	3,000
Clerical Assistant (50%)	1,000
Physician (20%)	1,400
Dishwasher and Custodian (50%)	500

2) Permanent Equipment:

Microscope, four objectives, binocular, moveable stage	\$1,000
Needles, bone marrow biopsy type, one dozen	25
Hemacytometers, AO "Brightline", five	87
Calculator, fully automatic, ten colum	950
Photoelectric spectrophotometer	308
Balance, analytic, automatic	875
Pipettor, automatic	360

3) Consumable Supplies:\$1,000

Media for microbiological assays, needles, syringes, rubber gloves, sponges, and miscellaneous medical supplies	1,000
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4) Travel:\$1,000

Transportation of staff to various hospitals, health centers and field stations within Trinidad.	600
Travel to scientific meetings in Caribbean Region.	400

5) Other Expenses :

\$ 600

Text books and other reference material dealing specifically with hematology	400
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5) Other Expenses (cont'd)

X ray film for diagnostic and follow up roentgenograms	200
6) <u>Total Direct Cost:</u>	<u>\$19,000</u>
7) Indirect Cost (15%)	<u>\$ 2,865</u>
9) Total Budget	\$21,965

Recommended Extension of Trinidad Program

Studies in the pathogenesis of anemia by morphologic and biochemical techniques require complementation with investigations which can best be performed using radioisotope tracer techniques, in particular, studies of the absorption and excretion of iron by  $\text{Fe}^{59}$ , measurement of total red cell volume by  $\text{Cr}^{51}$ , the measurement of iron incorporation into red cells using  $\text{Fe}^{59}$ , the measurement of red blood cell turnover with  $\text{Fe}^{59}$ , and the measurement of vitamin  $\text{B}_{12}$  absorption using  $\text{Co}^{58}$ .

BudgetPersonnel:

Physician (to maintain staff at full strength during specialized training, one at a time, of present staff).	\$ 6,000
Laboratory technician, chemistry	\$ 3,000
Part-time consultants	\$ 6,000

Permanent Equipment:

Scintillation counter, scaler and  
pulse height analyzer \$5,600

Consumable Supplies:

Purchase and delivery of radioisotopes \$ 500  
Glassware and safety equipment for  
handling isotopes \$ 500

Travel:

Transportation and per diem for  
physician and biochemist to 6 weeks U.S.  
Atomic Energy Course at Puerto Rico  
Nuclear Center \$1,400

Other:

Textbooks and reference material  
dealing with medical uses of radioisotopes \$ 300

Total Direct Cost: \$23,300

Indirect Cost (15%) \$ 3, 495

Total Budget: \$26,790

## II. CENTRAL AMERICA AND PANAMA

In Central America, much information is available regarding anemia from sick individuals seen in hospitals while suffering from a variety of illnesses. Methodology, however, has been quite variable so that intercountry and even intranational statistics cannot be compared. The need for a standardized survey of a randomly selected sample of population is evident. In addition, special surveys of randomly selected samples of so-called vulnerable groups such as pregnant and lactating women, preschool and school age children, workers performing heavy manual labor and the aged need to be performed. The surveys must include sufficiently sophisticated methodology to permit identification of major morphologic types of anemia. The identity of individual examinees should be retained in the event that more detailed pathogenetic studies such as those underway in the Caribbean might be carried out.

The following proposal has been prepared by the Institute of Nutrition of Central America and Panama (INCAP):

Title of Project: Study of Anemia Problem in Central America and Panama.

Institution: Institute of Nutrition of Central America and Panama, INCAP, Guatemala, C.A.

Survey of Hematological Values in Lactating Women and Pre-school Children, School Children and Selected Adult Groups.

Responsible Investigator: Dr. Carlos Tejada, Chief,  
Division of Pathology.

Background: While the experiences of physicians in hospitals and public health clinics throughout the area of Central America and Panama suggest that iron deficiency anemia is a major public health problem, there is at present no adequate knowledge of the true prevalence of this condition. Furthermore, there is reason to believe that macrocytic anemias of nutritional origin are also common and inseparably combined with the presence of microcytic anemia due to primary and secondary iron deficiency. The Institute of Nutrition of Central America and Panama (INCAP) has clarified other major nutritional problems in its ten years of existence, but it has not found it possible to undertake a systematic study of the problem of anemia, although this has been repeatedly recommended by its Technical Advisory Committee to be of major importance.

The data available would suggest that the groups most seriously affected are pre-school children and women of child-bearing age, while school children are not seriously affected in most areas. Even though the latter group, however, do not appear to have a high prevalence of anemia, school children studied in El Salvador and Guatemala showed a distinct tendency to macrocytosis by the methods employed. Although the surveys of school children in Nicaragua, Honduras, Costa Rica and Panama

are sufficiently indicative of a relative absence of anemia in this group, they are technically inadequate to permit classification of the anemia.

The problem of anemia in preschool children has been better studied and anemias has shown to be an almost constant accompaniment of kwashiorkor, which is very common in the area. Interestingly enough, in cases of kwashiorkor the proportion of anemias classified as macrocytic, normocytic and microcytic varies from one region to another. For example, in Guatemala City, cases are mainly normocytic or macrocytic, while in the coastal region of Tiquisate, they are more often microcytic. In San Salvador, the capital of El Salvador, the anemias in kwashiorkor are almost equally divided among macrocytic, normocytic and microcytic types.

Although a high percentage of women from lower socioeconomic groups in Central America and Panama are considered to be anemic when they are seen for prenatal visits, no systematic published studies are available. Records of the "Maternidad Carit" in San Jose, Costa Rica, indicate that women with red blood cell counts between one and two millions are not uncommon in their out-patient clinic and every year several ambulant pregnant women with red blood cell counts below one million are seen. These are stated to respond rapidly to the administration of iron, although in study done among pregnant women attended in the prenatal clinic of the main General Hospital in Belize, nearly all of the anemias were reported to be microcytic in type.

The physician presently in charge of this clinic states that over two-thirds of his patients are frankly anemic; he gives them iron orally and frequently uses in addition whole blood transfusions. It is obvious that present knowledge of the important problems of anemia during pregnancy is in a fragmentary and chaotic state and that systematic studies are required. Furthermore, the routine hemoglobin determinations that are done are limited to pregnant women so that nothing is known about either the effect of anemia on lactation performance or that of delivery and lactation on the severity of anemia.

A careful study of anemia in all members of the family carried out among 782 individuals in 137 families in the rural zone of Turrialba, Costa Rica, gave results similar to those indicated above and failed to find any relation between hookworm infestation and the type or severity of anemia (I-20). The techniques employed were not, however, well standardized.

It should be emphasized that the interpretation of the data collected up to the present time on the anemia problems in the area of Central America and Panama is limited by the fact that a variety of different methods have been used by different technicians and that standardization of methods and equipment have been generally inadequate.

Specific Aims: 1) To determine hemoglobin and hematocrit values in a random sample of lactating women as means of estimating the prevalence of anemia in all women of child-bearing age and of evaluating the effects of pregnancy and lactation on

hematological values; 2) to determine the type of anemia present by calculation of mean corpuscular hemoglobin concentration (MCHC) and examination of blood smears; 3) to determine prevalence of types of anemia in pre-school children by parallel studies in children 1-5 years of age at the same time the mothers are sampled; 4) determine prevalence and type of anemia in a random sample of school children in localities previously selected for the above; 5) carry out hematological surveys such as male agricultural workers and employees of selected industries as warranted by previous studies in more vulnerable groups.

Materials and Methods:

I.- Field Work: The following schedule will be used for the two years that the project is to last.

- A. Two months will be employed in each of the six Central American countries for a survey of anemia in lactating women and pre-school children.
- B. Four months more will be employed to repeat the same survey in opposite periods of the year in two of the countries to detect any major seasonal variation.
- C. The last eight months will be used to survey selected adult population groups and school children ( approximately one month in each of the Central American countries) and to evaluate findings.

II. The technique to be used will be as follows:

- A. The anemia survey in lactating women and pre-school children will be carried out by sampling families.

The Division of Statistics will select the villages that will be surveyed in order to obtain an appropriate sample of the country taking into consideration social, economical and geographical factors, as well as such parasitic infestations as hookworm and malaria. In each town, a record of the births which have taken place the year before will be obtained from the mayor's office and a personal home visit will be made of a random sample of these mothers. A finger tip blood sample will be taken from the mother as well as from her pre-school children. At the same time a questionnaire will be filled out to obtain information concerning the family.

- B. Seasonal variations will be studied by following the same procedures as the initial survey and two of the same villages will be revisited. The two countries to be rechecked will be those which in the first surveys were studied at the peak of the dry and rainy season, respectively; in this second survey the country will be visited during the opposite season.



C. The survey in adult and school children will occupy approximately one month in each country. Public schools shall be visited in the same towns selected for the previous studies and adult males from organized centers such as large farms near the villages will be chosen.

The questionnaires used during the sample collection will be the same type as used in the first part of the study.

### III. Laboratory Procedures:

- A. The blood will be examined in the field within three hours and the following determinations will be done:
- 1) Hemoglobin using the cyanmethemoglobin method with a portable photoelectric colorimeter.
  - 2) A microhematocrit as described by McGovern et al (8).
- B. A smear to be stained later at INCAP laboratories for final classification of the anemia in those cases where the hemoglobin is lower than 12 grams in women, 11 in children and 13 in adult males or the hematocrit lower than 37% in women,

35 in children and 40 in adult males.

- C. Enough blood will be collected from the finger tip into 6 x 75 mm tubes for micro determinations of vitamin A, carotene and cholesterol. The serum separated and refrigerated in the field will be sent to INCAP.
- D. Where indicated additional blood, bone marrow and urine specimens will be collected for diagnostic evaluation.
- E. Where indicated, serum paper electrophoresis for the detection of hemoglobinopathies.

IV. Personnel:

- A. Carlos Tejada, M.D., Chief, Division of Clinical Pathology, INCAP
- B. Guillermo Arroyave, B.S., Ph.D., Chief, Division of Clinical Biochemistry, INCAP
- C. Jose Mendez de la Vega, B.S., M.S., Ph.D., Chief, Division of Physiology, INCAP
- D. Miguel A. Guzman, B.A., M.S., Ph.D., Chief, Division of Statistics and Technical Services, INCAP
- E. Moises Behar, M.D., M.P.H, Director, INCAP

- V. Budget: It is recommended that a budget of \$59,573 be approved for this study at the Institute of Nutrition of Central America and Panama.

This budget may be itemized as follows:

Funds requested:		<u>1st year</u>
<u>Personnel:</u>		\$25, 140
Physician for direct supervision of program	6,000	
Consultants	6,000	
2 Technicians (Hematology),	6,120	
Laboratory staff:		
1 Medical Technologist (Hematology)	3,960	
1 Senior Technician (Serum Vitamin A and Carotene, microbiological assays)	<u>3,060</u>	
<u>Provident Fund</u>		1,508
<u>Insurance</u>		566
<u>Allowances</u>		1,508
<u>Travel</u>		6,789
<u>Supplies and Materials</u>		2,150
Glassware	800	
Chemicals	700	
Other supplies and materials	<u>650</u>	
<u>Freight and other Transportation Charges</u>		2,300
Air Shipments	300	
Operation of vehicles	<u>2,000</u>	

Equipment: 13,500

Mobile Unit

1 Vehicle, carryall or similar to be equipped as mobile laboratory and living quarters for staff	3,500
2 Colorimeters, \$500 each	1,000
1 Centrifuge	450
1 Refrigerator, kerosene type	400
1 Sterilizer, gas type	600
2 Cylinders, propane gas and lines	100
Paper electrophoresis apparatus	900
Refrigeration in laboratory, slide storage cabinet, rental of IBM card punching and sorting	2,600
Microbiological assay equipment	2,200
1 Generator, gasoline operated, 1 1/2 kw output capacity	600
Installation of equipment, reconditioning of vehicle	<u>1,000</u>

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\$ 51,803

Indirect Costs (15%)

7,770

\$ 59,573

### III. OTHER POSSIBLE PROJECTS

#### Mexico City

It is recommended that consideration be given to lending future support to the anemia study programs now being carried out at the Hospital de las Enfermedades de Nutricion in Mexico City.

#### Hematologic Investigations at High Altitudes

It is recommended that a consultant should be appointed to advise PAHO and WHO on lending support to hematologic studies at high altitudes. Such studies might be undertaken, for example, at the Institute for Andean Biology in Peru or by the Nutrition Division of the Ministry of Health, La Paz, Bolivia.

#### Puerto Rico

It is also recommended that funds be made available to the University of Puerto Rico, San Juan, to provide short-term fellowships for specialized training in modern techniques in hematology for scientists, both physicians and Ph.D.'s, and Baccalaureate-level technologists from laboratories participating in the anemia study program. A budget of \$7,200 is recommended for this purpose.

RECOMMENDATIONS FOR RESEARCH PROPOSALS  
ON THE EFFECTS OF NUTRITION ON PATTERNS OF GROWTH  
AND PSYCHO-MOTOR DEVELOPMENT IN CHILDREN IN LATIN AMERICA\*

A. Specific Aims

The purpose of this project is to investigate the physical and psychological development of children belonging to population groups having widely different genetic and cultural backgrounds and also living under different socio-economic and nutritional conditions.

B. Methods of Procedure

1. To secure a variety of nutritional and genetic conditions, typical communities in Latin American countries will be chosen for this longitudinal study. Initially those countries which have professionals especially trained in studies of growth and development\*\* will be selected, but as other countries fulfill these requirements, they, too, will be included. The groups to be studied will be selected from populations with different socio-economic, cultural, and environmental characteristics; and the specific criteria for selection will include the ethnic composition of the group, its degree of urbanization, the type of its economy, and its dietary pattern. Social-anthropologists, statisticians, and nutrition experts will provide technical assistance in the application of these criteria in determining the groups to be used for the sampling.

2. To chart the course of the physical and psychological development

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\*Prepared by Drs. J. Cravioto, G. Arroyave and M. Guzman of INCAP.

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\*\*At present Argentina, Colombia, Guatemala, and Mexico fulfill this requirement.

of the child in relation to its nutritional status, pregnant women and the babies born to them will be studied.

(a) The studies of pregnant women will include:

- i) Medical history and physical examination including, when possible, such biochemical determinations as hemoglobin and measurement of serum proteins.
- ii) Anthropometric measurements of the pregnant women, her parents and her husband, whenever practicable.
- iii) Evaluation of dietary intake.

(b) The studies of the children will include:

- i) Clinical examinations at regular intervals by a pediatrician seeking especially signs of nutritional deficiencies.
- ii) Anthropometric examinations, at specified intervals, following the recommendations of the Committee on Nutritional Anthropometry Food and Nutrition Board, and radiographs of the skull.
- iii) The following biochemical determinations have been chosen as being most informative regarding the adequacy of the protein nutrition.
  - a. 1) Creatinine excreted in the urine per unit of time, calculated per centimeter of body length or per kilogram of body weight (estimate of muscle mass development)
  - b. 1) The ratio of urea to creatinine in fasting urine specimens (as an indication of the relative rate of protein turnover, which, in turn, is

related to the level of protein intake.

- c. 1) Serum urea to contribute confirmatory evidence of the former
- d. 1) Quantitative determinations of the electrophoretic fractions of the serum proteins (to detect cases of relatively advanced protein malnutrition)
- iv) Bone maturation studies: radiographs of wrists will be made at 6-months intervals throughout the entire study.

v) Psychological tests:

As Goodenough and Harris have documented, the "search for a culture-free test, whether of intelligence, artistic ability, personal - social characteristics or any other measurable trait, is illusory; and the naive assumption that the mere freedom from verbal requirements renders a test equally suitable for all groups is no longer tenable". As the best compromise, the tests to be used will be those now employed by groups participating in the International Children's Centre studies. These are: The interview method, the Brunet-Lezine, or Gesell test, the Bayley test, the revised Stanford-Binet Intelligence Tests, and the Draw-a-Man Test of Goodenough. Fortunately in this study the effect of cultural bias on the conclusions will be minimized since, within each group selected, socio-economic characteristics will be similar despite the fact that there will be a consider-



able range in the severity of nutritional deficiency.

vi) Timing of examinations and tests:

The children will be examined at the following ages:

4 weeks + 2 days	39 weeks + 7 days
13 weeks + 7 days	18 months + 7 days
28 weeks + 7 days	2 years + 14 days

annually thereafter ± 14 days

The examination times are tentative and subject to modifications based on the preliminary findings, which may reveal the need for additional examinations or changes in the age period of the examinations in order to determine more accurately the points at which critical changes due to environmental factors occur.

vii) Dietary studies:

A Nutritionist will conduct longitudinal dietary studies. She will use, for that purpose, special forms to be designed on the basis of information obtained in preliminary family dietary surveys in the test localities. She will interview each mother selected for the project to learn her individual intake during pregnancy. Later, an attempt will be made to obtain an estimate of the amount of mother's milk that each child is ingesting. The total diet of the child will be studied each time the child is examined.

3. To relate the major features of the child's development to other relevant variables such as social background, size of family, state of health, parental education and mother deprivation, studies of the family and their social background and role in the community will be made each

year throughout the project. These will include:

- (a) Persons in the family and in the home, their ethnic group, their civil status, their age and relationship to the child, and their role and status in the group.
  - (b) The occupation and stability of the parents in their work, hours and length of work, use of free time, and the classification of the family according to its socio-economic condition following the method of Graffar.
  - (c) Education of both parents.
  - (d) Kind and condition of the dwelling.
  - (e) Beliefs and attitudes of parents regarding the relation of food and nutrition to health and disease.
4. To insure the success of the project several steps are necessary:
- (a) Additional capable professional personnel trained in studies of growth and development must be found. This will be done through preliminary correspondence and visits to the countries by one of the project directors.
  - (b) Techniques to be used in the study must be standardized. This can be accomplished through a workshop type of conference, attended by all principal investigators. Preceding the workshop background literature, descriptions of techniques, and material for analysis and interpretation will be distributed to all conference participants. Methods of collecting and interpreting data will be demonstrated, and the techniques to be used by technical personnel will be standardized. The problems connected with sampling, coding and making statistical analyses will also be demonstrated.

(c) Continuous assistance and guidance to ensure standardized collecting and evaluation of data must be carried on. A basic part of this project's plan is that either the principal investigator or one of the co-investigators of INCAP's "Growth and Development Project" will visit each cooperating group at least once a year to make certain that the conditions under which the data are collected are as nearly uniform as possible. Depending upon the degree of variability in conditions revealed by these periodic visits, collected material will be exchanged among different groups of workers for comparative interpretation. Workshops to discuss results obtained will be held every year at the project headquarters.

(d) It will be clearly understood throughout this project that the participating groups will be considered as independent research teams which have voluntarily adopted certain uniform methods of study. They will be free to publish their own results and will, in fact, be encouraged to make supplementary studies of their material according to their interests and opportunities.

C. Significance of this Research

Anthropometric measurements and patterns of growth and development are considered among the best indexes of the nutritional status of children. No country in Latin America, however, has accurate and reliable standards, and almost always the nutritionist must use either foreign standards or arbitrary figures. Debré has stated that all persons from the physician dealing with causes and effects of morbidity, to the states-

man seeking to influence social life, and to the economist trying to formulate a country's food policy-must begin with standards make possible comparisons of the past, the present and the future.

With international studies, an awareness from the beginning that the samples will differ in many characteristics and that direct comparisons are seldom possible is essential. Analysis of patterns and factors within a single sample can produce most valuable information regarding the influence of genetic, social, economic, and nutritional factors, and can thus provide the baseline indispensable for the evaluation of all other efforts to improve present adverse conditions.

Since a large proportion of the children living in technically underdeveloped countries suffer from protein malnutrition at some time during their pre-school years, it is important to have detailed knowledge of the immediate effects and sequela of various degrees of protein malnutrition. Preliminary results already obtained from cross-sectional studies in the community of Tlaltizapan, Mexico, indicate that retarded psychomotor performance of unknown duration is associated with the degree of malnutrition responsible for the retarded growth and physical development which are almost universal among lower income groups in most Latin American countries, Africa, India, and the Middle and Far East. Therefore, if this proposed study confirms previous findings that protein-calorie, malnutrition can cause retarded mental, as well as physical development, it would become even more important to apply emergency measures for the prevention of protein malnutrition in early infancy. It would lend fresh urgency to present world-wide efforts to develop new and inexpensive protein-rich foods and to use those already demonstrated as being practical. Instead of depending on long-term effects of agricultural improvement alone,

supplementary feeding programs for infants and pre-school children would receive an even higher priority. Hundreds of thousands of children could thus be rescued from preventable mental damage that could decrease their ability to absorb education and to realize their full potentials of contributing to the progress of their countries.

D. Background Information

Anthropometrical studies have revealed that in both rural and urban communities of technically underdeveloped areas where malnutrition is prevalent the average measurements of children at birth do not differ from those of the new born in more advanced regions. During the first 4 months of life, furthermore, growth rates of babies in those underdeveloped areas are satisfactory: and, if only weight gains are considered, they are equal or even may exceed the patterns established for normal North American or European children. After four months, however, the growth rate diminishes progressively, building up a difference from the normal which attains its maximum somewhere between 18 to 24 months. After this age the rate of growth apparently increases and starts to close the gap between the children of underdeveloped areas and their normal counterparts. The magnitude and especially the duration of this better growth, nevertheless, is not sufficient to enable these children to reach normal growth, so that at adolescence malnourished children are lighter and shorter than are normal children of the same ages.

Preliminary studies of the mental development of babies in the underdeveloped countries using the Gesell, Terman-Merrill, and Goodenough tests have shown that they are born with scores higher than the normal average, but these scores drop rapidly and reach subnormal levels at about 20-24 months. The deficit is about 30% at 42 months of age and

continues constant throughout school age into adolescence.

The mathematical relationship between the scores, expressed as percentages of the theoretical normal, and the chronological age in months are of the type  $Y = a + x^{-b}$ . Nevertheless good estimates were obtained using series of straight lines, as can be seen in the following table.

TABLE 1

Relationship between mental score (Gesell technique)  
and chronological age in months

Type of development (Y)	age periods (x)					
	birth to 12 months		12 to 24 months		24 to 42 months	
	y	SxY	y	SxY	y	SxY
Motor	137	2.61 x 19	124	1.36 x 13	88	0.15 x 15
Adaptive	143	3.77 x 22	116	1.21 x 11	89	0.008 x 12

The relationship between the intelligence quotient (Y) as determined by the Terman-Merrill technique, and the chronological age (X) gave the following regression equation calculated by the least square method for the period of 30 to 96 months of age:  $Y = 1.37 - 0.86 X$ ;  $SxY = 13$ .

Body weight and height were found to hold direct relationship to mental development scores, when age calculated on the actual height or weight, and not on the basis of chronological age, is plotted against the intelligence quotient.

The following equation describes this association: the intelligence quotient was found to be 0.79 times the "height age" plus 12, or 0.51 times the "weight age" plus 29. The errors of the estimates were 13 and

20 respectively.

Table 2 gives data on the correlation found between nutritional status, as judged by body weight and intelligence quotient, and as determined by the Goodenough test, in 299 school-age children.

TABLE 2

Relationship between body weight and intelligence quotient  
(Goodenough test) in 299 school-age children

% normal weight	No. of cases	Mean I.Q.
51-60	8	65
61-70	22	70
71-80	102	80
81-90	88	82
91-100	56	87
101-110	23	89

More interesting, perhaps, is the fact that while 20% of the children with normal weights gave scores between 60 and 70, 56% of the children with weights between 51% and 70% of the theoretical normal gave similar scores, and 3.33% of them did not even reach a score of 50.

Malnourished children are extremely susceptible to environmental factors and consequently are frequently admitted to hospitals after an infectious episode. Table 3 gives levels of behavior development on admission to the hospital and during recovery. It is important to emphasize that no complete normalization was achieved in a period of 15 weeks of treatment.

TABLE 3

Levels of behavior in children recovering from protein-calorie malnutrition (Values expressed as percentage of mean theoretical normal for chronological age)

Development	Days of treatment							
	0	15	30	45	60	75	90	105
Motor	39	47	47	54	57	59	62	66
Adaptative	36	51	53	65	69	66	66	71
Language	28	37	38	45	46	45	45	48
Social-personal	34	43	52	60	61	64	60	61

Although psychological changes accompanying severe malnutrition have been recognized for many years, the only study in which psychometric measurements of children suffering from kwashiorkor were made, as far as we know, was done by Geber and Dean in 1956. Twenty-five children admitted to the hospital in Kampala, Africa, with a diagnosis of kwashiorkor were placed under daily psychological observation and were given the Gesell test three times during their stay: on the first or second day of admission, one week later, and one month later. Their performance in the tests was poor at the outset, but they showed improvement as their physical condition improved.

No studies have been made of children considered normal in their villages, but who are mildly to moderately undernourished. Since these constitute the vast majority of children, it is of importance to investigate



the relation of their nutritional status to their mental development.

E. Specific Proposal

A better understanding of the relationship between dietary adequacy and the physical and psychomotor development of children will require meticulous long-term studies in representative population groups. These must include dietary studies, clinical examinations, anthropometric measurements, psychological tests and motor performance tests. Some children must be followed from birth to school age, and cross sectional studies should be done in carefully selected child populations of different ages whose socio-economic and nutritional history and status are known. At the present time the centers which have personnel trained and interested in such studies include:

I. Mexico: The group from the Hospital Infantil in Mexico City have pioneered such studies in the village of Tlaltizipan under the direction of Dr. Joaquin Cravioto and Dr. R. Ramos-Galvan. The studies are being continued under the supervision of Dr. Ramos-Galvan and could be expanded if additional financial support were available. A specific budget of current needs is not yet available. It is estimated, however, that this project should have at least \$20,000 additional support to extend the psychomotor retardation observations to other socio-economic groups in the area for comparison purposes and to pay for additional outside consultants for both the psychological testing and the anthropologic measurements.

II. Guatemala: Dr. Joaquin Cravioto has now become Chief of the Public Health Division of INCAP and has already begun a study to extend the observations initiated at Tlaltizipan along the lines described in the proposal (v.s.). An unusual feature of the study in Guatemala will be the opportunity to study an Indian community in which all children

under five have received substantial supplementary feeding for the past three years which will be continued. The minimum annual budget for this basic project is \$60,000 of which \$10,000 per year has already been obtained from the Nutrition Foundation. Requests for the additional minimum support required are pending with N.I.H. and another private foundation. If support is not obtained from these sources, PAHO should do everything possible to locate other sources of funds. If the minimum support required is obtained, and additional \$10,000 should be provided for consultant help in improving and standardizing the psychological testing procedures.

III. Colombia: It is probable that studies of this type can profitably be initiated in Cali with Dr. Canosa of the Department of Pediatrics, School of Medicine, Universidad del Valle. The budget required can be estimated from that given for the INCAP operation (v.i.). Supplementary funds would be required for outside consultant help in standardizing the psychological testing procedures, provision for the training of personnel at INCAP with Dr. Cravioto and for visits by Dr. Cravioto and Dr. Guzman of INCAP to Colombia to assist in setting-up and coordinating the study in that country. A budget covering these needs is appended (v.i.).

IV. Argentina: Dr. Marcos Cusminsky, Professor of Pediatrics at the University of La Plata, is deeply interested in carrying out a study of this kind and should be provided with the necessary consultant and financial assistance. A detailed budget can not be prepared at this time but can be estimated from that given for the INCAP studies (v.i.). In addition provision should be made for training one person at INCAP with Dr. Cravioto for three months and for Dr. Cusminsky himself spending one month at INCAP. Provision should also be made to permit Dr. Cravioto and

Dr. Guzman from INCAP to visit La Plata as part of one trip to Colombia.

A. budget covering these needs is appended (v.i.).

INCAP

Budget Proposal (first and subsequent years)

Personnel

Medical Officer, (Pediatrician)	IN-12	\$10,369	
Anthropologist	IN-12	10,369	
Assistant Psychologists (2)	IN-10	11,676	
Nutritionist (Dietary Surveys)	IN-10	5,307	
Clerk	IN-6	2,675	
Field workers (2)	IN-5	<u>4,816</u>	\$45,212

Travel and Transportation

Per diem for local travel	630	
Maintenance of a field vehicle	<u>1,200</u>	1,830

Supplies

Drugs for medical care	1,500	
Other field supplies	<u>600</u>	2,100

Meeting of Advisory Committee

Short-term Consultants fees, travel and transportation (10-day meeting)	<u>2,500</u>	2,500
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Equipment and Lodging Facilities

Vehicle (Volkswagen Microbus)	2,258	
Portable X-Ray Unit (including generator)	2,100	
Calculator	550	
Skin calipers, infantometers, pan scales and other physical examination equipment	600	
Materials for psychometric tests	500	
Construction of additional field work and lodging facilities	1,500	
Furniture, bedding and kitchenware	<u>850</u>	<u>8,358</u>

Total first-year operations \$ 60,000

It is believed that the project should continue for a minimum period of six years. The budget level for the second and subsequent years will not be lower since non-recurrent expenses (equipment and lodging facilities)

will be replaced by additional costs for personnel, data processing, publication of results, and for extending the study to an Atlantic Coast Caribbean Negro community.

Colombia Budget Proposal, Supplemental to Estimates Derived from INCAP

Two consultant psychologists (three months, two round trip air fares, Bogota-New York and 90 days per diem)	\$4,600
Two trainees for training at INCAP (three months, air fares Colombia-Guatemala and return and per diem)	3,000
Consultation visits of INCAP personnel to Colombia (three round trip air fares Guatemala-Colombia and per diem)	1,400
Total	\$ 9,000

Argentina Budget Proposal, Supplemental to Estimates Derived from INCAP

Trainee for training at INCAP (three months, air fare round trip La Plata-Guatemala and per diem)	\$1,462
Visit of Dr. Cusminsky to INCAP (one month, air fare round trip La Plata-Guatemala and per diem)	1,611
Consultation visits of INCAP personnel to Argentina (two air fares round trip Bogota-La Plata and 20 per diem)	2,492
Total	\$ 5,565

The above general proposals for studies of the effect nutrition on the patterns of growth and psychomotor development of children have been prepared by the INCAP Staff, principally, Dr. Joaquin Cravioto, Chief of the Public Health Division, Dr. Guillermo Arroyave, Chief of the Division of Physiological Chemistry, and Dr. Miguel Guzman, Chief of the Division of

Statistics. It is based on extensive field experience in Mexico and Central America with these types of studies and on discussions of the problem held with a group of outstanding authorities selected for their knowledge of psychological testing, studies of psychomotor development, physical and nutritional anthropometry, epidemiology and clinical and public health nutrition. The latter meeting was held at the University Club, New York City, on April 13, 1962, under the auspices of the Nutrition Foundation.

RECOMMENDATIONS FOR RESEARCH ON THE INTER-  
RELATIONSHIPS BETWEEN NUTRITION AND INFECTION  
IN COLOMBIA, CHILE AND BRAZIL

The two types of studies in this area are exemplified by the following which are continuing in INCAP under the technical responsibility of Dr. Nevin S. Scrimshaw as consultant director:

1.- Effect of Infection on the Nutritional Status of Children

Children with a variety of acute and chronic infections are being studied by metabolic balance techniques to determine the degree to which additional losses of nitrogen, calcium, vitamin A, ascorbic acid, and other nutrients occur. Children with severe intestinal parasite burdens are similarly studied before and after treatment. Significant adverse effects of yellow fever and smallpox vaccines as examples of very mild viral infections are being found. About \$40,000 annual for five years is available for this work.

2.- Field Studies of the Interrelationship between Nutrition and Infection

Morbidity and mortality from all diseases in children under five years of age is being studied in three rural highland Indian villages by bi-weekly visits to every family and each child is examined periodically to measure growth and maturation and to determine nutritional status. One village serves as a control; and in a second an intensive nutrition education and experimental feeding program is

maintaining the children under five in a relatively good nutritional state. In the third village children are treated specifically or symptomatically for every infection and every effort is made to prevent infections by immunizations, latrine construction and other environmental sanitation measures and health education.

The specific aim is to demonstrate the reduction in the severity of infections in children who are well nourished and the improvement in nutritional status of children who are not under severe infectious stress. The experiment which is in the third year of a planned five year study at a cost of approximately \$100,000 per year is proving successful in achieving the first aim and partially successful in the second. In addition, a great deal of extremely useful data on the epidemiology of diarrheal and other infectious diseases in these communities are being obtained.

It will be noted that these studies are expensive and technically difficult. Many individuals have talked about doing such studies and physicians from Chile, Brazil, Peru and Colombia have received training in INCAP partly designed to prepare them for conducting studies for this purpose. While PAHO is not ready at the present time to designate those individuals and locations where either of the two types of research listed can be carried out, the support of such studies on a pilot scale should receive a high priority in PAHO research program.

- 3 -

RECOMMENDATIONS.- It is specifically recommended that a suitable consultant be requested to visit those persons and institutions which have expressed an interest in such studies or who might reasonably be helped to initiate them. Dr. Rueda-Williamson in Colombia, Dr. J. Harpa in Chile and Drs. Dutra and Gandra in Brazil are four of the individuals with the greatest potential for such studies. The sum of \$3,000 should be sufficient for the consultant trip envisaged. It is recommended that PAHO budget or obtain the sum of \$50,000 a year for two years to support such studies in their early phase.

END