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**A PROGRAM FOR COLLABORATIVE RESEARCH  
IN THE NUTRITIONAL ANEMIAS  
IN LATIN AMERICA**

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

A PROGRAM FOR COLLABORATIVE RESEARCH IN THE NUTRITIONAL ANEMIAS  
IN LATIN AMERICA\*

The general questions which one would like to have answered in the following discussion concerning anemia in the Americas are: 1) the magnitude of the anemia problem; 2) the type of anemia prevalent; 3) reasons for the existence of certain anemias in specific geographic areas; and 4) what can be done to reduce the incidence of anemia. The present discussion will attempt to summarize the limited information available about the frequency and types of anemia and to outline an approach to the unanswered questions.

Incidence

The incidence of anemia is poorly defined in Central and South America and in the Caribbean. One source of information is from practicing physicians who have an impression of the frequency of severe anemia in the hospital population. Another source of information comes from nutritional surveys conducted jointly by the individual countries and the Interdepartmental Committee on Nutrition for National Development of the United States. Such surveys have been carried out in Peru (December 1959), Ecuador (July 1960), Chile (August 1961), Colombia (September 1961), West Indies (June 1962), and Uruguay (May 1963). Finally, there are various publications from Latin America dealing with anemia; few of these, however, are concerned with incidence studies. A general statement which summarizes well the present information is taken from the report of the WHO Scientific Group on Research in Nutritional Anemias which met in Caracas, September 1963. "A review of the current literature has shown an appalling

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lack of factual information on the incidence and etiology of nutritional anemias although it is generally accepted that they constitute one of the major public health problems in most developing countries in the tropics and subtropics. This was particularly so for countries in Latin America and the Caribbean." Anemia is known to be prevalent in the islands of the Caribbean, in Colombia, and in rural communities of limited economic means in Mexico, Venezuela and other countries. For example, in Trinidad, forty percent of the adult females had hemoglobin levels of less than 12gm percent, and the average hemoglobin values in men and women were about 2gm below the accepted normal (1). In studies on pregnant women from the low income group in Mexico, a 38% incidence of anemia was observed (2). An attempt was made to summarize the status of each country in reference to anemia at the Caracas meeting (3), but information was so meager as to have little meaning.

### Etiology

If it may be assumed that anemia is a problem of sufficient importance to merit investigation, the cause of anemia next bears scrutiny. Here there is good indication of the great importance of iron deficiency. For example, studies now being carried out under USPHS sponsorship in Trinidad by Dr. J. Chopra shows that pregnant women with anemia almost invariably have low serum iron and a reduction in the percent saturation of transferrin to a level diagnostic for iron deficiency anemia. In Bogota and Medellin in Colombia, the great majority of severe anemic patients have iron deficiency anemia. In a recent study carried out by Dr. Y. Gandra at the head of the Amazon River, the majority of patients with anemia responded to iron. In rural populations in Venezuela, Roche and Layrisse found iron deficiency anemia in high prevalence.

In all of these areas where iron deficiency anemia is conspicuous, there is known to be a high incidence of hookworm infestation. Some of the most important studies on the role of hookworm deficiency anemia have come from Puerto Rico, Brazil and Venezuela. The early studies of Oswaldo Cruz (4) and of Rhodes and associates (5) clearly establish the importance of hookworm in the production of a negative iron balance through bleeding. More recently, Roche and associates (6) have made a careful study of the quantitative relationship between the size of the hookworm load and the amount of iron lost. For each thousand eggs per gram of feces there is a loss of about 0.6 mg of iron. The susceptibility of any given individual would then depend on the parasite load and the amount of iron available in the diet. In surveys of dietary iron, the intake according to accepted standards is adequate except for Trinidad and Colombia, where average daily intake is about 10 mg. However, there is reason to question the adequacy of the diet since most of the iron is derived from vegetable sources and recent studies suggest that this form of dietary iron may be poorly absorbed.

Evidence concerning other types of anemia is fragmentary. Megaloblastic anemias have been reported in malnourished children in Jamaica and in Cali, Colombia, and in pregnant women in Colombia and Venezuela. These are probably due to folate deficiency although differentiation from B<sub>12</sub> deficiency with modern assay methods has not been carried out. Hemoglobinopathies and metabolic defects of the red cell have been shown to exist but to date are not known to be of great importance as compared to the deficiency anemias. Protein deprivation which is prevalent in certain areas of Central and South America has not been included as a cause of anemia for there is little evidence that it produces anemia in a physiologic sense. While surveys show average

hemoglobin values of one or as much as two grams below normal in the malnourished population, there are no instances of severe anemia due to protein lack. The hemoglobin fall seems, if anything, proportionately less than the wasting of other tissues. Recent studies by Reissman (7) have shown that the decrease in erythropoiesis accompanying protein starvation is due to a decrease in erythropoietin stimulation of the marrow rather than a change in the functional capacity of the marrow itself.

One may summarize these remarks on incidence and types of anemia to suggest that there is a great prevalence of iron deficiency anemia in the Western Hemisphere and that the majority of this is due to interaction between the blood loss of hookworm infestation and the restricted diet imposed by economic limitations. It remains yet to be determined whether megaloblastic anemia as a reflection of either folate or B<sub>12</sub> deficiency, hereditary disorders including hemoglobinopathies and red cell metabolic defects will assume general importance. The serious limitation of information at present available is undoubtedly due to a number of factors including the limited scientific personnel working in the field and the many other responsibilities which they carry, which limit the time for investigation, and the meager laboratory facilities and financial support for fostering research on anemia. These conditions have resulted not only in inadequate information but in much of the data collected being of limited value.

#### Prevalence studies

In 1958, the World Health Organization called together an expert committee to explore the problem of how to obtain more critical information in the geographic area where anemias were prevalent. A table of values for the normal

individual was accepted and anemia was defined. It was decided to focus initially on iron deficiency anemia and various proposals were explored by consultants travelling to South America, Africa and Asia. The program of study which evolved examined simultaneously the incidence of iron deficiency anemia and looked into various explanations for its cause. Protocol studies were set up and the cooperation of a limited number of laboratories was elicited including those of Ramalingaswami in Delhi, Bothwell in Johannesburg, Roche and Layrisse in Caracas and Finch in Seattle. The incidence of iron deficiency anemia was evaluated by 1) studying the pregnant women in the third trimester as a highly sensitive indicator of the vulnerability of the population to iron deficiency and 2) evaluating iron reserves by analyzing the non-heme iron content of pieces of liver obtained at necropsy. The etiology of iron deficiency was examined in three respects: in the first place, more detailed studies were undertaken concerning the relationship between hookworm load and iron deficiency anemia. In studies on a rural Venezuelan population Layrisse and Roche have shown an increased incidence of anemia only when the hookworm load exceeds two thousand ova per gram of stool. In adult man a load of over five thousand ova per gram of feces was required to produce an increased incidence of anemia. A second study was carried out to determine whether iron losses were greater in the tropical areas than had been observed in temperate regions. Groups of subjects were injected with  $\text{Fe}^{55}$  and blood samples are being obtained over a period of several years. From the fall in activity, iron loss in sweat and other excreta can be determined. The third approach deals with the nutritional value of food items. Through the radioactive labeling of different types of food, wheat has been studied in Seattle, beans in Caracas, and corn in Cairo. Results to date indicate that the availability of wheat iron is far less than that of salts.

or of iron derived from meat. Data obtained in the various studies have been summarized in a WHO report (9).

Recently WHO has expanded its interests to include other nutritional anemias and in particular B<sub>12</sub> and folate deficiencies. In designing an effective approach to these three types of anemia, it became apparent that standard hematologic procedures designed to characterize anemia such as cell indices, reticulocyte counts, blood smears, and marrow aspirations, were costly, cumbersome and non-specific. On the other hand, chemical and microbiologic assays on plasma reflected deficiencies of these substances in the individual, were precise and adaptable to population survey, and were far less expensive than hemotologic workups. Accordingly it was proposed to study the incidence of deficiency of folate, B<sub>12</sub> and iron by plasma assays rather than to deal with the differential diagnosis of anemia. The specific procedures which appear to be most useful are the percent saturation of transferrin as a guide to iron deficiency, the serum B<sub>12</sub> level determined by the Euglena assay, and the serum folate determined by the L. casei assay. The pregnant woman and the child between the age of one and two were selected as sensitive groups which would be particularly likely to point up deficiencies existent in the general population.

The next step was to establish machinery whereby these studies could be applied to remote areas where such information would be most important. It seemed essential that figures obtained would be accurate and comparable from one region to another. It was decided that this could best be accomplished by the establishment of regional centers to which a number of investigators could send samples. Current plans are to establish such regional centers at Caracas, London, and Johannesburg. Attention is being given to standardization of methods between these different laboratories and to the details of shipping

procedures of samples from the field and finally to details of population sampling. With this background in respect to the WHO program, it now seems worthwhile to focus on Latin America and the Caribbean and to indicate what has taken place to date and what might seem desirable in the future.

#### Proposed program

In September of 1963, a conference was called in Caracas by WHO, involving research workers in Latin America and the Caribbean along with consultants and officials of WHO and PAHO (3). At this meeting the WHO program as it had evolved thus far was discussed, and there was agreement by all that a regional center should be established. Caracas was considered the best place both from the standpoint of the capabilities of the laboratory and its general location. At present, support is being sought for the establishment of this center. A number of the individual participants to the conference were also stimulated to apply for support of their own programs, but these were not closely tied in with the general program.

Since September, plans for the development of the center have progressed. The special procedures to be carried out in this center have been set up and samples are being exchanged with other reference laboratories for the purpose of standardization. During the first year, trials are proposed involving a study in the Caracas area under Layrisse, and in Trinidad under the direction of Chopra. The execution of these studies, and the processing of samples in Caracas will provide opportunity to work out all of the details for the co-operative program. It would seem that in addition to studies on iron, B<sub>12</sub>, and folate levels of the serum, it would be worthwhile to include hemoglobin electrophoresis and determination of glucose-6-phosphate dehydrogenase in the



erythrocyte. The additional procedures would be economical and would increase the information which would be gained from sampling various populations. Plans are made for the training of collaborating physicians and technicians at the center in Caracas during the coming year. The auspices of the Pan American Health Organization will be most helpful in providing fellowships to promising individuals for broader training in the United States.

During the coming year it will be important to identify regional participants who may join the center's program and carry out the necessary population sampling from their own areas. It seems desirable that emphasis be placed on young men who do not have an extensive commitment of other sorts and who would be willing to take on this responsibility for a period of time. It would seem necessary that some local facilities be available and that there also be assurance locally that the individual will be given the necessary support. In the present program it is not the intent to provide initial support to these individuals beyond the technical services of the center, the necessary training for the physician and his technicians, and minimal supplies for drawing blood and for mailing costs. Most of the original studies will be carried out in urban areas. Significant financial support may be required for rural studies which would be expected to lead to more important findings. However in the initial phase, when effective collaborators will be identified and trained, it is felt that most of the special work can be carried out in the center. As information accumulates which points to local problems in anemia of some importance, specific studies can be developed in those areas to clarify the particular problem.

Anemia, poorly defined as it is in Latin America and the Caribbean, without question is a public health problem of some magnitude and one which requires more than a "hit or miss" approach. The present facilities and

potential for undertaking such studies are most inadequate where they are most needed. The proposed program would permit the collection of accurate scientific information and provide a training center for scientific personnel. The essential feature yet to be identified is a group of participants with the proper scientific background who will pursue these necessary studies in their own countries.

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