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STUDY GROUP IN ENDEMIC GOITER IN LATIN AMERICA

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STUDY GROUP IN ENDEMIC GOITER IN LATIN AMERICA\*

The study group on endemic goiter in Latin America began its work in 1962. Beginning with investigators from laboratories in Mexico, Ecuador, Chile, Brazil and Venezuela, the program now includes representatives from laboratories in Columbia, Peru and Argentina. Three congresses of participants have taken place since the initial organization. The first of these was in Caracas in 1964, the second was in Mexico in 1966, and the third was held in June of 1968 in Puebla, Mexico. The deliberations of the third congress are just now being published by the Pan American Health Organization. This compendium of 34 scientific papers includes the significant research on endemic goiter and related defects which has been accomplished by the participants in the past year or two. These congresses have profited from the contributions and advice of investigators who have studied endemic goiter in New Guinea, central Africa and other parts of the globe.

Most of the participating laboratories have active and ongoing programs for research into the problems of endemic goiter. Funding has become increasingly difficult, but no program has been without some support, and in some instances the success of the program has enabled the laboratory to obtain support from local governmental sources. In addition in some, if not all instances, the success of the programs has enabled the investigators to expand the scope of their laboratory operations and to attract into their orbits the bright young men of the local medical community.

This summary report includes a brief recapitulation of recent results, current activities and research projections for the near future.

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Argentina

Dr. O. J. Degrossi of the Center for Nuclear Medicine of the Hospital de San Martin and of the Faculty of Medical Sciences of the University of Buenos Aires has recently joined the program. His present studies may be divided into two. He is engaged in comparing the effects of iodized oil in normal subjects when given intramuscularly and orally. This is part of an effort to determine the optimal way for administering the oil. His second project is an iodized oil prophylaxis program among the Indians of Chiquillihuín in central western Argentina. Dr. Degrossi and his group have made extensive surveys and physiological studies on these isolated Indians, who are not far removed from those of the Pedregoso region studied in recent years by Barzelatto in Chile. Dr. Degrossi has four young research associates engaged in his research activities on endemic goiter.

Brazil

There are two foci of activity in Brazil. One of these is under the direction of Dr. Luis Carlos Lobo, now Dean of the Faculty of Medical Sciences at the University of Brasilia. Near Brasilia are several districts with endemic goiter. In cooperation with personnel from the University of Sao Paulo Dr. Lobo has conducted extensive surveys of the population groups in these areas in relation to thyroid disease. Detailed family and social data have been accumulated and collated for analysis. In the course of these surveys a number of goitrous and non goitrous cretins have been identified. Dr. Lobo and his group now intend to measure thyroid function in detail in these subjects and to compare them with normal individuals living in the same areas. He also intends to extend his studies on social and sanitary conditions of living in relation to goiter prevalence. In conjunction with these investigations he is also studying the effect of thyroidectomy on the development of the nervous system in rats. A growth and development group associated with his medical school is now starting longitudinal study of mental development in children in relationship to thyroid function of the mother during pregnancy.

Dr. Geraldo Medeiros-Neto at the Hospital das Clinicas of the University of Sao Paulo has studied the distribution of iodinated proteins in the thyroid of patients with endemic goiter and has also made and published some physiological observations on certain subjects with deafmutism and goiter from the Sao Paulo district. Availability of human thyroid tissue at surgery in his hospital has enabled Dr. Medeiros to project extensive studies on the biochemistry of these thyroids.

Chile

The group in Chile is directed by Dr. Jose Barzelatto, who is presently assigned to Washington on a governmental mission. In his absence the program is directed by his associate Dr. Carlos Stevenson. Together with his collaborators Drs. G. Pineda and E. Silva he is studying the effect of iodide deficiency on hyperthyroidism. They seem to have an unusually large number of patients who have usual plasma organic iodine concentrations and postulate that this is largely triiodothyronine. The investigators are also studying the effects of iodide deficiency in the rat on kinetics of iodoaminoacid synthesis and turnover in the thyroid and on turnover rates and volumes of distribution of triiodothyronine and thyroxine.

Colombia

The principal thrust of activities by this group has been toward a definition of the epidemiology of endemic goiter in the region and a search for the etiological factor or factors. The investigation has been under the direction of Dr. Eduardo Gaitan. Although Dr. Gaitan is spending the current year in the laboratory of Dr. Grant Liddle in Nashville, his program continues with the help of Dr. Jorge Gaitan and Dr. MacLennan. These investigators have become increasingly convinced that there is an active goitrogenic substance in water obtained from certain shallow wells. They have made considerable progress in concentrating and characterizing this goitrogenic factor. It seems to be volatile, sensitive to peroxide and soluble in organic solvents. It has not yet been chemically characterized. It may be a product of bacterial growth in the wells. Whether its concentration in drinking water is sufficient to alter thyroid hormone synthesis remains to be proven.

These investigators are carrying out an extensive survey of a 500 square mile area of the Cauca Valley. Measurements include goiter prevalence, quantity of iodine in urine, thyrotropic hormone in plasma, thyroid hormones in plasma, and antithyroid antibodies. The major effort for the near future will be toward determining the chemical nature of the suspect goitrogen from water of the region, developing methods for measuring the goitrogen in water and biological fluids, attempting to find techniques for inactivating the goitrogen in water supplies, and performing physiological studies on the effects of the natural goitrogen on thyroid function in man and animals. Dr. Eduardo Gaitan returns shortly to Cali, but it is problematical whether his long time associate, Dr. Wahner, will return from his present post at the Mayo Clinic.

Ecuador

Studies on endemic goiter in rural Ecuador continue at an active pace. These are directed by Dr. Rodrigo Fierro and his associates. Present interest centers principally on the long term effects of an iodinated prophylactic oil program. This was begun in the spring of 1966. Recent surveys have indicated the effectiveness of the iodinated oil in preventing endemic goiter, and statistics presently seem to indicate that it is effective in preventing the appearance of deafmutes and cretins in the population group. There is no clear evidence thus far that linear growth or bone maturation is influenced, but there is statistical suggestion that intellectual performance is improved. Because of the importance of this last observation a parallel and similar study has been started in a village where endemic goiter is severe and defective persons are common.

The program is reasonably well financed at present. Now that the iodinated oil study has been in effect for three and a half years the time is fast approaching when there should be definite and unequivocal information about the effectiveness of iodinated oil in preventing endemic cretinism, deafmutism and mental retardation in an area where these have been spectacularly common in the past. During the past year the program has been considerably strengthened by the application of modern statistical methods. Dr. Robert MacLennan of Tulane University has spent many weeks in Quito and in the villages working with Dr. Fierro and transcribing all the accumulated data to punch cards and developing programs for their analysis.

The program has been unusually successful in attracting the interest and participation of medical students and young graduates of the

medical school in Quito. One of these after spending two years as the medical officer in the villages is now on fellowship at the University of West Virginia. He has been replaced by another graduate of the University of Quito who in his turn should have an opportunity for a research fellowship in an appropriate laboratory and clinic. These well trained young men expect to return to Quito to join in the laboratory of Dr. Fierro and broaden its base.



Mexico

Since its inception this program has been under the direction of Dr. Jorge Maisterrena of the Hospital de Enfermedades de la Nutricion. In addition to a continuing collaboration with Dr. Enrique Tovar, each year Dr. Maisterrena has had a medical student working as an active participant in the endemic goiter study. Until recently the activities centered around the town of Tepetlixpa where Dr. Maisterrena had developed a small laboratory. Over the years the prevalence of goiter has slowly fallen, evidently as a result of the introduction of exogenous foods. Surveys just completed during the current year have indicated a continuing fall to only 8% in children in the 6 to 7 year age group but a slight rise in older children. Because of the changing pattern of thyroid disease in Tepetlixpa the group has now shifted its activities to Xicalco a small town not far from the new quarters of the Instituto Nacional de la Nutricion. Here the prevalence of goiter seems to be reasonably high and the possibility of studies excellent. Dr. Maisterrena intends to pursue the possibility that goitrogenic agents in local food and water may play a role in the endemic. Acquisition of new equipment enables measurements of radioactive iodine with as small a dose as one microcurie and long term observations with 10-20 microcurie doses.

Peru

The activities of the Peruvian group under the direction of Dr. Eduardo Pretell are in three villages in the neighborhood of Tarma, west of Lima, in the Andean highlands. A control study of the effectiveness of iodinated oil in goiter prevention was begun by Dr. Pretell in the fall of 1966. Epidemiological studies have disclosed the effectiveness of the program in reducing the incidence of goiter and in preventing its appearance in newborns. A finding of unusual interest was that there was no rise in the concentration of thyroid hormone in the blood of patients with endemic goiter during pregnancy, but that a normal rise occurred if the subject had received an injection of iodized oil.

Dr. Pretell is keeping a careful epidemiological account of the progress of the population groups involved in this study with particular reference to goiter incidence and the fate of newborns who come into the program. He also intends to continue his studies on the function of the thyroid of the patients treated with iodized oil. He is obtaining information on the rate at which the iodized oil is released and the way in which this correlates with plasma hormone levels and radioactive iodine uptake and turnover. He has as an associate a recent graduate of the medical school in Lima and is making every effort to obtain the assistance of other young physicians and students in the course of his investigations. He works as an integral part of the Institute of High Altitude Studies in Lima at the Universidad Cayetano Heredia.

Venezuela

During the past year an extensive survey of medical problems of some of the remote Indian groups in southern Venezuela was accomplished by a joint effort of IVIC and a delegation from France under Professor Comar. There was no active participation of PAHO in these studies and no formal publication has yet come to attention. Dr. Gaede and his group at IVIC continue their observations on thyroxine synthesis and the enzymology of the thyroid gland. The remoteness and inaccessibility of the endemic areas make continuing investigations of their medical problems most difficult.

Discussion

The Pan American Health Organization program on endemic goiter in Latin America falls naturally into two divisions of effort. One of these is concerned with research into problems of prevalence, etiology, pathophysiology and health impact. The other relates to preventive measures and measurement of the effectiveness of these. While there is a certain incompatibility between these two goals in the sense that effective prevention would preclude the possibility of further study, at the practical level there is no risk that in the foreseeable future there will be any lack of opportunity for research on virgin endemic goiter in Latin America.

The two principal studies with prophylaxis by iodized oil have given entirely comparable results. In both, effectiveness has been proved, feasibility demonstrated and lack of unacceptable toxic effects ascertained. Observations in the areas of Ecuador and Peru where these studies are in progress are incomplete in showing the long term effects of iodized oil in preventing endemic cretinism, endemic mental deficiency, and endemic short stature. Statural growth has not been dramatically affected by the oil program. There are suggestive observations favoring an effect on mental development and strong reason to suspect that cretinism is eliminated. The rate at which newborns are entering the study groups will make it possible to answer these questions with finality in the next year or two provided suitable support continues and the interest of the principal investigators is sustained. There appears to be no doubt that both conditions will be met.

The results of the iodized oil prophylaxis program have seemed sufficiently convincing to warrent extension of the method to other

areas of Latin America where there is little probability of effective salt iodization in the near future. Ideally, implementation of these preventive programs would be preceded by thorough surveys of the proposed areas and careful followup in order to obtain further information on effectiveness.

Abundant opportunities for research remain. The most provocative finding is that of Gaitan in Cali of an identifiable goitrogenic substance in the water from certain wells. When methods have been developed for detecting this factor in water, his findings should be extended to other areas where endemic goiter exists and where iodide lack seems not to be a completely adequate explanation for the presence of the disease or where the disease has not been eradicated by prophylactic measures.

There continues to be a need for further studies on alternative sources of goitrogenic agents in relation to endemic goiter. The findings of goitrogens in casava in Nigeria and a curious geographical (but not dietary) distribution of endemic goiter in the Kivu lake district of the Congo both attest to the possibility of dietary goitrogens in need of identification.

Little is known of the factors which control the relative quantities of triiodothyronine and thyroxine formed and secreted by the thyroid in relation to endemic goiter. Several investigators have pointed out that patients with low levels of serum protein-bound iodine in endemic goiter regions may appear to be clinically euthyroid. This has been attributed to a relatively high concentration of triiodothyronine, but this remains to be proved. Furthermore, if this is true, factors which determine the relative proportions in which these hormones are secreted remain to be determined. Investigations along these lines require highly refined biochemical

methods and access to thyroid tissue at the time of surgery. There are several centers in Latin America where these conditions co-exist.

The emergence of highly refined and sensitive methods of assay for the hormones of the pituitary, the adrenal, gonads, parathyroid and pancreas now make it possible to appraise the dynamic state of the endocrine system at an entirely new level. It will be of immense interest to apply these, as has already been done to a limited degree, in the study of the adaptive processes to iodine deficiency, the cretinous state and the growth retardation accompanying severe endemic goiter.

Clearly much remains to be done, both at the level of epidemiological surveys and prevention, and in laboratory and field research related to the etiology and pathophysiology of endemic goiter. The investigators of the Pan American Health Organization study group on endemic goiter are responding to these challenges.