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PROPHYLAXIS OF ENDEMIC GOITER BY IODIZED OIL IN  
RURAL ECUADOR

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## PROPHYLAXIS OF ENDEMIC GOITER BY IODIZED OIL IN RURAL ECUADOR\*

Goiter was known among the Indians of the Andean world before the Spanish conquest. The recent discovery of pre-Columbian clay figures showing goiter testifies to the commonplace nature of the disease before the coming of the white man. Today in many isolated villages and towns of Columbia, Venezuela, Ecuador, Peru, Bolivia and Chile goiter is found in a large fraction of the population. Where endemic goiter is severe many persons with cretinism, deafness, mutism, short stature and varied other neurological deficiencies are seen. The precise relationship between endemic goiter and these other afflictions has never been quite clear.

A survey by the National Institute of Nutrition of Ecuador in 1958 disclosed that endemic goiter is a grave problem in the Andean region. It was noted that the prevalence of goiter varied widely among neighboring villages and that many of the defective persons with deafness, mutism, and so on did not present the characteristic aspects of hypothyroidism. The results of studies of iodine metabolism were consistent with a deficiency of iodine as the principal causative factor of the endemic. For various reasons including economic strictures iodinated salt has not been widely distributed in the country and is hardly used in the rural communities.

This paper is a report on the incidence and pattern of endemic goiter in two typical impoverished Andean villages of Ecuador and a preliminary account of the results of a pilot program designed to assess the effectiveness of iodized oil in prevention of goiter and of those disabilities which accompany it in a highly endemic region of Ecuador. The prophylaxis program was inaugurated in

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March 1966. The most recent full survey was in April of 1968.

Endemic goiter has been a focus of considerable medical interest in Ecuador for many years. An inventory of the total population of a number of villages has disclosed the magnitude of the endemic and has revealed much information on the ecology and sociology of these people. Two villages were singled out for the study described here because of their proximity to each other, geographical and social isolation, socio-economic immobility, and high incidence of endemic goiter and defective persons. One of these, Tocachi, has a population of approximately 900, while LaEsperanza, 4 miles away, has approximately 1400 inhabitants. Most of the people live on small farms. The daily diet is fundamentally vegetarian based on barley, corn, potatoes and other tubers. Most have meat only once or twice in each month. Such salt as is available is a crude preparation prepared on the coast from sea water.

The size of the thyroids was evaluated in accordance with the usual Pan American Health Organization classification. Thus, Grade OA: non palpable; OB: palpable, (more or less the size of the terminal phalanx of the thumb of the person examined) but not visible with the head raised; Grade 1: easily palpable with head in normal position and visible with the head raised; Grade 2: easily visible with the head in normal position; Grade 3: visible at a distance; and Grade 4: huge goiters. For a diagnosis of cretinism the fundamental fact taken into account was the mental deficiency of the subject as was obvious to the surveyor and confirmed by the habitus and manner of life in relation to the rest of the community. Considerable difficulty was encountered in attempting to assess the degree of mental competence in the population as a whole and especially those with disability such as deafmutism. This was compounded by

the social and intellectual deprivation of the community as a whole, and pointed up the need for application of highly sophisticated methods of appraisal which would be independent of formal education or acquaintance with the mainstreams of western culture. These factors coupled with linguistic difficulties and a native reticence has made evaluation difficult indeed. Some indication of the socio-economic status of these two villages may be obtained from Table 1.

A number of studies were done prior to the iodinated oil prophylaxis program in order to demonstrate the pattern and distribution of endemic goiter and to document the pathophysiology of the thyroid in these patients (Table II). Deficiency of iodine was indicated not only by the low level of stable iodine excreted daily in the urine but also in terms of the elevated avidity for iodine as indicated by the high mean radioactive iodine uptake. The conversion ratio for  $I^{131}$  was high and the  $PBI^{131}$  was also elevated. The  $PBI^{127}$  on the average was somewhat low in both villages. There was virtually no iodine in the water or salt available to the two populations.

Both diffuse enlargements of the thyroid and nodular goiter were age related (Fig. 1). A significant incidence of both was found below age 5 and this increased until the fifth decade, when there was a sharp increase in the incidence of nodular goiter at the expense of diffuse goiter. These figures are perhaps not particularly meaningful since it is very difficult to appreciate the presence of nodules in some patients with seemingly diffusely enlarged thyroids. Administration of iodide will often lead to involution of the hyperplastic elements and reveal nodules which were not previously apparent to the examiner.

Categorization of the defective persons in these two villages has proved to be a difficult task. One may classify these persons into several categories according to type and degree. Thus, some subjects may have mental deficiency and deafmutism, others may have these two findings in addition to short stature and spastic motor abnormalities. Others may be deafmutes but at least superficially appear to have normal intelligence. Even the typical cretin, i.e., severely mentally retarded patient with short stature and characteristic facies and gait may vary in terms of hearing ability, stature, chondrodysplasia, and degree of spastic neurological abnormalities. For present purposes there seems to be little profit in a detailed classification according to sub groups. In a larger series of studies encompassing a number of villages, there has been a clear correlation between cretinism and other forms of retardation and the prevalence of nodular goiter.

Cretinism appeared not to have a family predelection. Cretins did not group within families, and no difference was found in the frequency of endemic goiter in a particular village in families with or without cretins.

The protein bound iodine concentration tended to be low but was not uniformly low in patients with overt cretinism. One family group was of unusual interest. A patient with classical cretinism and a large nodular goiter came for examination with her mother and father, both of whom had large nodular goiters. The patient brought along her 16 months old infant. The child was hypothyroid and was severely retarded. Serum thyroxine iodine concentrations on all four members of the family group were below 1, except for the father of the cretinous mother. His was 2.7. The father of the infant was unknown.

The program for the study of endemic goiter prophylaxis by intramuscular administration of iodized oil was begun in March 1966. During a ten day period 90% of the population of Tocachi were injected with Ethiodol, a preparation which is 37% by weight of iodine. Each ml containing 475 milligrams of iodine. Children up to two years were injected with 0.2 ml, children up to six years with 0.5 ml, children up to twelve with 1.0 ml and adults with 2.0 ml. The control group has been the inhabitants of LaEsperanza. A representative group of children from each of the two villages was studied for dental development, weight, height, head circumference, and bone age by hand x-rays. A physician and a midwife have been resident in both villages since March 1966. They have been responsible for prenatal care and for postnatal followup of all children born since that time. They have been particularly concerned with somatic growth and neuro-motor development. Epidemiological surveys have been conducted every six months on goiter incidence, thyroid function, and urinary excretion of iodine. In addition in April of 1968 virtually all subjects of the 1966 program were reexamined for goiter incidence and size, somatic growth, dental development, and bone maturation by hand x-ray. In addition data were collected on psychic and neural status on a representation group of children from the iodized oil group and the control group. Full analysis of these data are incomplete at the present writing.

The only immediate reaction to iodide injections was a single instance of transient local erythema. At the time of the first follow-up survey six months after administration of Ethiodol several subjects were identified who seemed to have symptoms suggestive of thyrotoxicosis. They were taken to Quito, hospitalized and carefully examined both clinically and by laboratory testing. Administration of the iodinated oil had limited specific diagnostic tests to measurement of the butanol extractable iodine and <sup>131</sup>I triiodothyronine resin uptake test. The diagnosis of thyrotoxicosis

was confirmed in three patients. All were older women with large nodular goiters. All three were started on a program of methimazole administration, 15 milligrams three times a day. This resulted in prompt remission in two of the patients in two or three months and the thyrotoxicosis has not recurred. One patient was still thyrotoxic eighteen months later. She had taken methimazole only intermittantly. Measurements of urinary excretion of iodine, protein bound iodine concentration in the serum, butanol extractable iodine concentration and butanol insoluble iodine concentration were all elevated for two years after the beginning of the ethiodol program. Radioactive iodine uptake fell to low levels following injection of ethiodol but rose slowly and was within normal limits a year later on the average. It was interesting to note that the radioactive iodine uptake of a small sample of persons in Tocachi who had not received injections also became normal. This was attributed to the fact that huge amounts of iodine had been excreted by the injected villagers and had been incorporated into the food by contamination and fertilization of the soil

Successive epidemiological surveys have shown a progressive reduction in the goiter incidence in Tocachi and a small but significant increase in the control population in LaEsperanza. The reduction has been most striking in the large multinodular goiters. There has also been a relative increase in the Grade 1 nodular goiters at the expense of Grade 1 and Grade 2 diffusely enlarged glands. The reason for this presumably is the enhanced delineation of small nodules resulting from involution of hyperplastic glands which seemed diffusely enlarged but in fact they contain nodules. A larger percent of children are without goiter in the ethiodol group than before or in the control population. A number of older women in the ethiodol group now have redundant loose skin in the neck which previously was stretched taut over large multinodular goiters.

The most important aspect of the ethiodol program is the effect which it might have on development of children born into the program. At the time of the April 1968 survey 177 children were born in LaEsperanza since March of 1966. Seventeen (9.6%) had died and five (2.7%) had left the area. Eighty-one of these (45%) were conceived after the program was begun. In Tocachi 90 children had been born, of whom sixteen (17%) had died and two had gone away. Of the 90, fifty-six were conceived within the program. Assessment of mental deficiency, hearing loss and motor development is difficult in this age group. The findings which follow can be accepted as tentative only pending more time and full analysis of our data.

Somatic growth of children both in Tocachi and LaEsperanza is retarded. This is evidenced both by comparison with values from a high income class of children in Quito and with a low income class group from the maternity hospital also in Quito. All groups are delayed when compared with data from European and American sources. Head circumference of children from Tocachi born into the program is slightly higher than that of children of comparable age and sex in LaEsperanza.

Dental age in both villages is retarded. Neurological maturation stages are met at an older age than in American and European children as published by others. The maturation delay so far seems to be somewhat longer in children from LaEsperanza than in those in the Ethiodol program from Tocachi, but in some aspects the maturation is the same in both groups.

Three instances of severe mental retardation have been found in LaEsperanza. One of these is a typical cretin already mentioned above, one has Down's syndrome and the third is unclassified. While



infants with some degree of retardation have been found in Tocachi, none has been found who is so severe as those encountered in LaEsperanza.

Summary:

1. Endemic goiter with attendant cretinism, mental deficiency, deafmutism, short stature and neuromuscular retardation is a major medical problem in many rural communities in the Andean world.
2. Two villages in Ecuador have been chosen for a pilot project to determine the effectiveness of intramuscular administration of iodized oil in the prevention of endemic goiter and related disabilities. Ethiodol (37% iodine) was injected into approximately 900 villagers and the adjoining village serves as a control. A resident physician and midwife have major responsibility for accumulating detailed data on the development of all children born into the program.
3. There has been one instance of transient local erythema following the injection. Three subjects developed thyrotoxicosis after administration of the ethiodol. All three were older women with large nodular goiters. Two of these have been successfully controlled with methimazole; a third who has taken her methimazole only intermittantly remains thyrotoxic.
4. There has been a sharp reduction in the incidence of goiter in the iodized oil group. This has been particularly true of the incidence of large nodular goiters and of the appearance of goiters in the young. There has been a relative increase in the incidence of small nodular goiters. This is thought to be a result of in-

volutionary changes in hyperplastic goiters which permit better delineation of nodules which were missed in previous surveys.

5. The observations to date encourage the impression that neuro-muscular growth and development are better and severe retardation less frequent in the population group which had received the ethiodol.

6. Administration of ethiodol to large population groups is technically feasible, safe and effective in the control of endemic goiter. Results up to the present time enable us to advise an extension of the use of ethiodol to larger population groups. The occurrence of thyrotoxicosis in older patients with large nodular goiters suggests that these patients should be given smaller doses of ethiodol or that they should be excluded from the program.

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TABLE I

	TOCACHI	LAESPERANZA
% of Subjects born in the village	97	91
% of infant mortality	43	29
% of unwed mothers	26	14
% of illiterate Subjects	31	34
% Subjects who have visited the coast region	5	9
% of artisans	5	5
Annual Income per capital (\$)	90	85
General Endemic Goiter, %	54.4	53.0
Nodular Endemic Goiter, %	48.0	34.0
Diffuse Endemic Goiter, %	6.4	17.0
Mental Deficiency & Deafmutism, %	7.4	5.5
Mental Deficiency, Deafmutism, Shortness & Motor Abnormalities, %	0.8	0.5
Deafmutism, %	4.53	2.58
Mutism, %	0.40	0.41
Deafness, %	1.06	0.00
Motor Abnormalities, %	1.06	0.83
Other Congenital Malformations, %	0.40	1.25



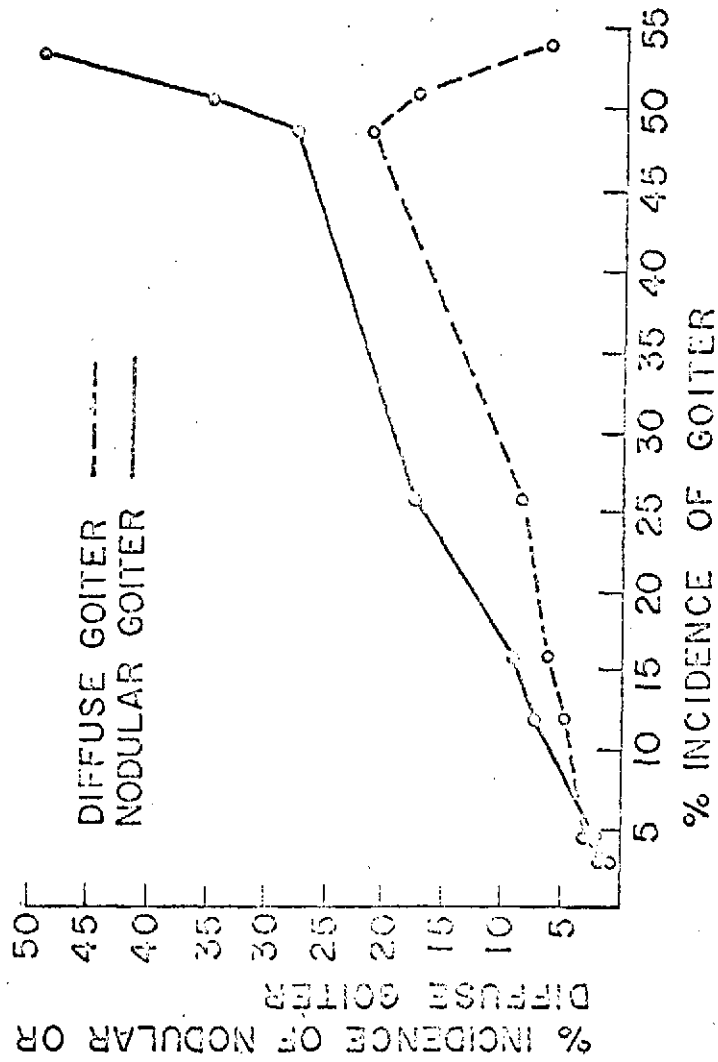


Figure 1