and R. W. Lam. Use of 8-anilino-1-
-sulfonic acid (ANS) in radioim-
of triiodothyronine (T_3) in unex-
ım. *Am Fed Clin Res* XX: 216,

?. Delange, J. Goldstein-Golaire, and
ans. Endemic goiter prevention by
a reassessment. *J Clin Endocrinol*
1196-1204, 1973.

y our criteria they would still be
in reason we think deaf-mutism
cretinism syndrome is that we
ıd it in the normal population,
subjects with other features of
would say that endemic deaf-
not be an entity to be con-
ely from endemic cretinism. We
' that if you want to do quick
population, there will be good
:retinism if you find impaired
ı tones of more than 40 decibels.
n with cretinism is 92 per cent.
The whole field of this associa-
l by the fact that in any popula-
going to find an occasional
d an occasional patient with
mpairment. Such patients might
ion to endemic cretinism. It is
fficult to recognize such patients
re there is known endemic cre-

l would like to challenge Dr.
ement that deaf-mutism is a good
er for cretinism. Last summer I
he Uele region in Africa, where I
00 people and found a prevalence
atous cretinism of 1.5 per cent.
:e of deaf-mutism was only 0.1 per
s the same as might be expected in
ulation in any region of the world.
this example deaf-mutism should
ırded as a universal tracer for
inism.

THE ROLE OF IODINE IN INTELLECTUAL DEVELOPMENT IN AN AREA OF ENDEMIC GOITER

RODRIGO FIERRO-BENITEZ, M.D.,* IGNACIO RAMIREZ, M.D.,*
EDUARDO ESTRELLA, M.D.,† AND JOHN B. STANBURY, M.D.‡

Well-documented studies on endemic cretinism have demonstrated that this disorder is found in geographic association with endemic goiter (*1-6*). Traditionally, the term "endemic cretin" has been applied to subjects with obvious mental retardation and defects in hearing, speech, and walking. As has been demonstrated in the Ecuadorean Andes (*6, 7*), the incidence of endemic cretinism is related more to the socioeconomic situation of a community than to the magnitude of its iodine deficiency. The following questions, among others, remain to be answered: What is the extent of intellectual deficiency in areas where endemic cretinism is highly prevalent? Can iodine deficiency, which may lead to cretinism, also cause less obvious intellectual deficiencies? What time factors are involved in the effects of iodine deficiency on intellectual development? These questions are particularly important when we consider that areas of endemic cretinism usually harbor, in addition to iodine deficiency, protein-calorie malnutrition, cultural deprivation, and adverse socioeconomic and sanitary conditions.

The study presented here is part of a program to prevent goiter by the administration of iodized oil in an endemic area of rural highland Ecuador (*8, 9*). It was designed to evaluate the role of iodine in intellectual development in areas of endemic goiter, i.e., the role of iodine in *endemic mental retardation*, including both obvious and more subtle degrees of mental retardation.

*Department of Radioisotopes, National Polytechnic School, Quito, Ecuador.
† School of Medicine, Central University, Quito, Ecuador.
‡ Unit of Experimental Medicine, Department of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, Massachusetts.

Several general observations indicated to us the need for such a study. We carried out an epidemiologic inventory of the total population of eight rural villages in those provinces of the Ecuadorean Andes which are most affected by goiter (*3, 7, 10, 11*), and demonstrated a close relationship between the serverity of the endemia and the incidence of cretinism. In that survey we regarded mental deficiency as the most distinguishing feature of the cretin. To support this diagnosis, we required that mental deficiency be obvious to the examiners and be confirmed by the manner in which the subject lived in relation to the rest of the community. By this we mean that his family would consider him incapable of performing the normal activities of the average inhabitants of his village, such as agricultural tasks and minor crafts. This criterion was employed because many residents of these communities exhibit a degree of simplicity and naivité in comparison with urban dwellers. The surveyors had the strong impression that rather than two absolute and discrete conditions, there was a continuum in levels of intelligence from "normal" subjects to those diagnosed as cretins.

The present study is presented as additional support for such a continuum. It is based on studies of two groups of subjects in two of the previously studied communities, Tocachi and La Esperanza. These were done on a "defective group" of 77 persons ranging from 9 to 60 years of age, including almost everyone who had obvious abnormalities in walking, speech, hearing, and mental capacity, separately or combined, and a "normal group" of 50 adults chosen at random or by intention, including local leaders, artisans, farmers, and servants. In these two groups intelligence was scored by

using adaptations of the Gesell, Leiter, and Binet-Simon tests, the first two for the subject who was deaf or mute (*12*). By the Stanford-Binet classification (*13*), the "defective group" scored in the idiocy, imbecility, mental weakness, and borderline defective categories. The "normal group" scored in the mental weakness, borderline defective, low average, normal, and high average categories. Thus, overlapping was found between the "defective group" and the "normal group" when they were compared in terms of mental age and IQ's (Table 1). The results indicated also that in these communities a significant percentage of the "normal" population could, in fact, be classified as mentally weak or borderline defective. Nevertheless, there are inherent difficulties, which we recognize, in any direct comparison of these IQ values with those obtained in another culture.

Two periods during embryogenesis are important in considering the effects of iodine deficiency on intellectual development. One is the first 8 weeks of gestation, when the central nervous system begins to form and develop (*14*). The other is the initiation of fetal synthesis of thyroid hormones, which occurs at about the 12th week of intrauterine life (*15*).

In the present study we were aware that intelligence is an elusive entity and that under any conditions intelligence tests are only estimates of mental capabilities. Furthermore, assessment of intellectual capacity presents additional problems when one is working across cultural barriers among persons largely deprived of educational opportunities and for whom social contacts are limited or vitually nonexistent.

SUBJECTS AND METHODS

This study was conducted in Tocachi and La Esperanza, two remote and entirely comparable neighboring rural Andean communities (*8*). Severe chronic iodine deficiency, protein-calorie malnutrition, and a high prevalence of goiter and cretinism are the most important characteristics of these Spanish-speaking villages.

In March 1966, every person in Tocachi was injected with iodized oil. In December 1968, all women of childbearing age were reinjected and all children born after 1966 were injected. La Esperanza remained the control village. Details of this iodine supplementation program and of ongoing studies have been reported elsewhere (*8, 9, 16-18*).

The children born in Tocachi during the seven-year period of the study were divided into two groups:

Tocachi Group 1: Children in whom correction of iodine deficiency occurred between the fourth to seventh month of fetal life directly by intramuscular injection of the mother.

TABLE 1. Distribution of "defective" and "normal" persons from Tocachi and La Esperanza, Ecuador, by IQ's in the Stanford-Binet classification.*

Intelligence quotient (IQ)	Defectives (No.)	Normals (No.)	Classification (Stanford-Binet)
0-19	35		Idiocy
20-49	40		Imbecility
50-69	1	9	Mental weakness
70-79	1	22	Borderline defective
80-89		5	Low average
90-109		13	Normal or average
110-119		1	High average

*Terman, L. M., and M. A. Merrill, *Stanford-Binet Intelligence Scale*, Houghton Mifflin Company, Boston, 1962.

Tocachi Group 2: Children
iodized oil prior to conce

The children from La Esp
whom received iodine, were gr

La Esperanza Group 1:
matched by age and se
child in Tocachi Group
than one child was avai
particular child in Tocac
tion was used.

La Esperanza Group 2:
matched by age and se
child in Tocachi Grou
random selection when n

The principal test used was
the Stanford-Binet Intelligence
adaptation involved picture
vocabulary with local characte
for ages 2 through 9 years w
translated into Spanish by a
dorean physicians who had w
and La Esperanza for more t
had a good knowledge of the
habits, and speech patterns.
tested were at least 36 months
failed to successfully comple
ford-Binet items for the 2-ye
latter children, three were fro
1, one from Tocachi Group
Esperanza Group 1, and thre

**TABLE 2. Numl
of p of t**

Group
Tocachi Group 1
La Esperanza Group 1
Tocachi Group 2
La Esperanza Group 2

*Spiegel, M. R. *Sta*

Tocachi Group 2: Children of mothers given iodized oil prior to conception.

The children from La Esperanza, none of whom received iodine, were grouped as follows:

La Esperanza Group 1: Children pair-matched by age and sex, one for each child in Tocachi Group 1. When more than one child was available to match a particular child in Tocachi, random selection was used.

La Esperanza Group 2: Children pair-matched by age and sex, one for each child in Tocachi Group 2, again with random selection when necessary.

The principal test used was an adaptation of the Stanford-Binet Intelligence Scale (*13*). The adaptation involved picture recognition and vocabulary with local characteristics. The tests for ages 2 through 9 years were adapted and translated into Spanish by a team of Ecuadorean physicians who had worked in Tocachi and La Esperanza for more than 10 years and had a good knowledge of the villages' customs, habits, and speech patterns. All the children tested were at least 36 months of age, but some failed to successfully complete all the Stanford-Binet items for the 2-year level. Of these latter children, three were from Tocachi Group 1, one from Tocachi Group 2, four from La Esperanza Group 1, and three from La Esperanza Group 2. For them, items from the Catell Infant Intelligence Scale were used to establish the baseline at which all test items could be completed successfully. Once established, this baseline was used for scoring in the same manner as the baseline established with the Stanford-Binet items. Other details of the methods used in this study have appeared in three preliminary reports (*19-21*).

A total of 216 children were tested: 103 (60 males and 43 females) in the treated village, Tocachi, and 113 (57 males and 56 females) in the control village, La Esperanza. Only children who manifested appropriate behavior during examination were included. We rejected those who refused to cooperate at any time during the test. These consisted of five from Tocachi Group 1, two from Tocachi Group 2, and eleven from the two La Esperanza groups. Most of these rejected children were reexamined one year later (five in Tocachi Group 1, two in Tocachi Group 2, and eight in the La Esperanza groups). Also rejected were one boy and one girl (twins), on the grounds of extremely poor physical condition and severe malnutrition; they would have belonged to Tocachi Group 2.

RESULTS

As shown in Table 2, the mean IQ score in Tocachi Group 1 was 71 and in La Esperanza

TABLE 2. Number, sex, mean IQ scores and range, SD and "Z" Test* value of p of the children tested from Tocachi and La Esperanza.

Group	Number M	Number F	IQ Mean value (range)	SD	"Z" Test Value of p
Tocachi Group 1	24	16	71.72 (41-101)	14.6	No sig.
La Esperanza Group 1	26	24	69.16 (42-105)	13.3	
Tocachi Group 2	36	27	83.66 (55-105)	13.4	$p < 0.002$
La Esperanza Group 2	32	31	72.74 (40-105)	14.0	

*Spiegel, M. R. *Statistics.* McGraw-Hill, Mexico City, 1970, 169 pp.

Group 1 it was 69. This difference was not significant. In Tocachi Group 2 the mean IQ value was 83, and in La Esperanza Group 2 it was 72, a highly significant difference ($p < 0.002$).

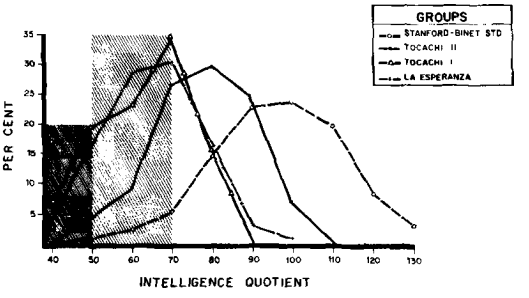
Since children with IQ scores below 70 are considered mentally retarded, many children in both villages must be regarded as mentally defective (Table 3). However, only 9.5 per cent of the children in Tocachi Group 2 scored in the mentally defective range. Furthermore, in this group there were no children scoring below 50, the range corresponding to idiocy-imbecility. The lowest IQ's in Tocachi Group 1, La Esperanza Group 1, and La Esperanza Group 2 were 41, 42, and 40, respectively. Not a single subject had an IQ below 20, the range corresponding to idiocy. The highest IQ was 105, found in children belonging to Tocachi Group 2 and in both La Esperanza groups.

When the distribution of IQ scores of each group is charted (Figure 1), the curves of Tocachi Group 1 and of both La Esperanza groups tend to be skewed in the direction of mental deficiency, while the curve of Tocachi Group 2 has a clear tendency toward normal.

DISCUSSION

Three facts emerge from our findings: 1) The general performance of the children was poor. 2) The spectrum of intellectual capacity was wide, covering practically all mental categories. 3) The children in whom chronic iodine deficiency was corrected prior to conception showed less intellectual impairment.

FIGURE 1. Distribution of IQ scores within each of the study groups from Tocachi and within the combined groups from La Esperanza.



Note: The Stanford-Binet standard is given for comparison. The darkly shaded area corresponds to the "idiocy-imbecility" category, the lightly shaded to "mental weakness."

We have presented elsewhere the limitations of the methods of intellectual assessment used in this study (*19, 20*). Nevertheless, there are good reasons for believing that the poor general performance of the children did not reflect difficulty in comprehension of the test beyond that expected from their low intelligence. More than 70 per cent of the children comprehended the tests and completed them satisfactorily. A greater number of children in Tocachi Group 2 performed the tests successfully. Furthermore, the results obtained in the children were quite similar to those found in adults of the same communities, except that defective adults had lower IQ's than the lowest IQ's found in children. This might be partly explained by the severely deprived conditions under which the mentally retarded live in these communities (*21, 22*).

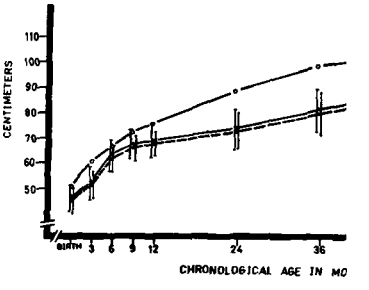
TABLE 3. Distribution of IQ scores for each group of children tested from Tocachi and La Esperanza.

IQ	Tocachi Group 1		La Esperanza Group 1		Tocachi Group 2		La Esperanza Group 2		Classification Stanford-Binet
	No.	%	No.	%	No.	%	No.	%	
90-109	4	10.0	3	6.0	21	32.8	10	15.8	Normal or average
80 -89	9	22.5	7	14.0	20	31.7	9	14.2	Low average
70 -79	11	27.5	15	30.0	16	25.3	22	34.9	Borderline defective
50 -69	13	32.5	21	42.0	6	9.5	19	30.1	Mental weakness
0 -49	3	7.5	4	8.0	–	–	3	4.7	Idiocy and imbecility

The poor general intellectua
these children, including even
Group 2, may be considered in
nutritional and environmenta
They live in communities in w
daily diet does not reach 1,9(
sumption of animal proteins
These conditions have bee
worsening for generations (2
development of children from
retarded in relation to that o
children from developed count
illustrated in Figures 2 and 3.

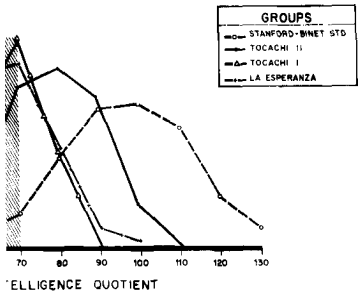
Additional understanding
occurring during the growing
gained from a consideration
This measure is not constant in
increments in growth vary w
Height increases rapidly during
followed by a period of decele
9, at which time it accelera
adolescence. As illustrated in F
difference can be noted on co
curves of Tocachi and La Esp
curve established by Wilkins
American children. Not only is
Ecuadorean children generally
deceleration stage is more pro
critical period from the first to t
life. In this period, growth is go
by genetic factors but by
environmental ones as well (2
life and particularly during the

**FIGURE 2. Height (mean ± st
from birth to 5 years, of children bo
La Esperanza during 7-year period of**



Note: Comparative values for
United States are taken from Nelson

Distribution of IQ scores within each roups from Tocachi and within the s from La Esperanza.



Stanford-Binet standard is given for e darkly shaded area corresponds to ecility" category, the lightly shaded to ss."

esented elsewhere the limitations ls of intellectual assessment used (*19, 20*). Nevertheless, there are for believing that the poor general of the children did not reflect omprehension of the test beyond from their low intelligence. More ent of the children comprehended completed them satisfactorily. A er of children in Tocachi Group 2 e tests successfully. Furthermore, tained in the children were quite ose found in adults of the same except that defective adults had han the lowest IQ's found in might be partly explained by the ived conditions under which the rded live in these communities

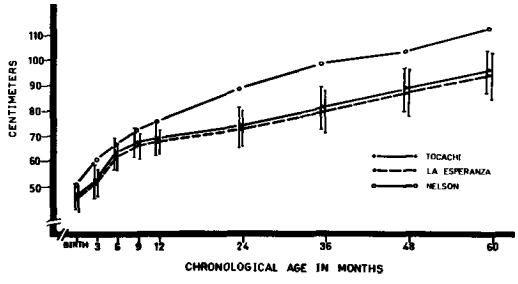
hildren tested from

Esperanza Group 2 %	Classification Stanford-Binet
15.8	Normal or average
14.2	Low average
34.9	Borderline defective
30.1	Mental weakness
4.7	Idiocy and imbecility

The poor general intellectual performance of these children, including even those of Tocachi Group 2, may be considered in relation to their nutritional and environmental circumstances. They live in communities in which the average daily diet does not reach 1,900 calories. Consumption of animal proteins is minimal (*8*). These conditions have been progressively worsening for generations (*23*). The physical development of children from both villages is retarded in relation to that of well-nourished children from developed countries (*24, 25*), as illustrated in Figures 2 and 3.

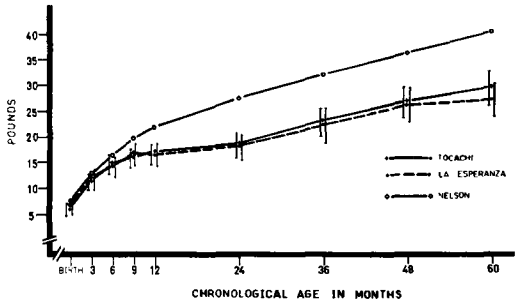
Additional understanding of the changes occurring during the growing period can be gained from a consideration of growth rates. This measure is not constant in the child, since increments in growth vary widely with age. Height increases rapidly during the first year, followed by a period of deceleration until age 9, at which time it accelerates again with adolescence. As illustrated in Figure 4, a great difference can be noted on comparison of the curves of Tocachi and La Esperanza with the curve established by Wilkins (*25*) for North American children. Not only is the rate of the Ecuadorean children generally slower, but the deceleration stage is more pronounced in the critical period from the first to the third year of life. In this period, growth is governed not only by genetic factors but by nutritional and environmental ones as well (*26*). During fetal life and particularly during the first two years

FIGURE 2. Height (mean ± standard deviation) from birth to 5 years, of children born in Tocachi and La Esperanza during 7-year period of study.



Note: Comparative values for normals in the United States are taken from Nelson (*24*).

FIGURE 3. Weight (mean ± standard deviation) from birth to 5 years, of children born in Tocachi and La Esperanza during 7-year period of study.



Note: Comparative values for normals in the United States are taken from Nelson (*24*).

of postnatal life, nutritional factors have important physical, chemical, and functional effects on the human brain (*27-30*). Severe limitations during this period lead to exaggerated responses to certain stimuli, poor ability to extinguish responses, and decreases in cognitive and perceptual development. Perhaps a great deal more could be said if one could determine the effects of alienating forces, such as cultural deprivation and the precarious physical and emotional condition of the family, on the total development of the child. Some of these factors are explored in the studies of Cravioto *et al.* on rural Mexican children (*31*).

FIGURE 4. Annual increment of height from birth to 5 years of males born in Tocachi and La Esperanza during 7-year period of study.

Note: Comparative values for normals in the United States are taken from Wilkins, L. A., *Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence*, C. C. Thomas, Springfield, Ill., 3rd ed., 1961.

In this study we noted levels of intelligence that ranged from normal to the obviously retarded with IQ's below 50. If, by convention, we define endemic cretins as those with a mental capacity at the idoicy-imbecility level, we can state that correction of iodine deficiency before conception prevents endemic cretinism. On the other hand, correction of iodine deficiency after the third month of intrauterine life appears to have no effect on future intellectual ability, at least under the conditions of our field trials. This suggests that the mental development of a child may be dependent on maternal thyroid function during embryogenesis or perhaps, as a working hypothesis, that it may be related to an extrathyroidal action of iodine on the development of the central nervous system during early embryogenesis. Possibly maternal thyroid function may be important to adequate placentation.

Endemic cretinism has not been reported in areas where, despite severe chronic iodine deficiency, the diet is adequate or in places where, despite severe protein-calorie malnutrition, the iodine supply is adequate. The present work indicates that iodine deficiency is a necessary condition for the appearance of endemic cretinism in a community. Whether it alone is a sufficient condition for endemic cretinism cannot be answered at present.

Even in Tocachi Group 2, a significant number of children showed mental retardation. This suggests that factors other than iodine deficiency play a role in their intellectual development. When intellectual deficiency persists in areas of endemic goiter after correction of iodine deficiency, other causes should be searched for, particularly protein-calorie malnutrition.

SUMMARY

This study assesses the effects of prenatal iodine administration on intelligence in children from an iodine-deficient area of rural Ecuador. In one village, Tocachi, all inhabitants were injected with iodized oil in 1966. Two years later, all children born since 1966 were injected and all women of childbearing age were reinjected. A neighboring village, La Esperanza, provided untreated controls. The children of Tocachi were divided into two groups: Group 1 had been exposed to adequate iodine supply beginning at the fourth to seventh fetal month, while in Group 2 adequate iodine had been available from the moment of conception. The children of La Esperanza were divided into two groups to correspond chronologically with those of Tocachi. An approach to intellectual assessment was conducted, using the Stanford-Binet Intelligence Scale as modified by the authors.

The mean IQ values for Tocachi Group 1 and for the two groups from La Esperanza ranged from 69 to 73, with no significant differences. Group 2 from Tocachi had a mean value of 84, which was significantly greater than its control group in La Esperanza ($p < 0.002$). In Tocachi Group 2, no child had an IQ below 50, in contrast to the other three groups.

If cretins are defined as subjects with mental capacities at the idiocy-imbecility level (i.e., obvious mental retardation), provision of adequate iodine supplies from the time of conception onward appears to prevent endemic cretinism.

ACKNOWLEDGMENTS

The help of José Suárez, M.D., and of Edgar Viteri, Víctor Espinoza, and José Reinhart, medical students, is gratefully acknowledged.

The studies related to endemic cretinism in Ecuador were sponsored by the Pan American Health Organization, the United States National Institutes of Health, the United States National Association for Retarded Children, and the Public Health Ministry of Ecuador.

(1) Dumont, J. M., A. M. E Bastenie. Thyroidal func demic. IV. Hypothyroidis tinism. *J Clin Endocrinol* 1963.

(2) Choufoer, J. C., M. van Rhi Endemic goiter in wester Clinical picture, incidence endemic cretinism. *J Clin* 25: 385-402, 1965.

(3) Fierro-Benítez, R., W. Peñaf and I. Ramírez. Endemic cretinism in the Andean re 280: 296-302, 1969.

(4) Buttfield, I. H., and B. S cretinism in eastern New to goiter and iodine defici S., and P.O.D. Pharoah, ec *ism.* Monograph Series N Human Biology, Papua, N pp. 55-69.

(5) Delange, F., A. M. Ermans, Endemic cretinism in Idjwi Zaire Republic). In Stanbu Kroc, eds. *Human Deve Thyroid Gland: Relation t ism.* Plenum Press, New 87-113.

(6) Ibbertson, H. K., J. M. Tait, R. McKinnon, and M. cretinism. In Stanbury, J. I eds. *Human Development Gland: Relation to En* Plenum Press, New York, 1

(7) Fierro-Benítez, R., L. DeG Suárez, and W. Peñafiel. cretinismo endémicos en la Ecuador. *Rev Ecuat Cien B*

(8) Fierro-Benítez, R., I. Ramír Jaramillo, C. Díaz, and J. U in the prevention of en associated defects in the Ecuador. I. Program design prevalence, thyroid functio cretion. *Endemic Goiter.* tion No. 193. Pan Americar tion, Washington, D.C., 196

(9) Kevany, J., R. Fierro-Benítez, J. B. Stanbury. Prophylaxis endemic goiter with iodi Ecuador and Peru. *Am* 1597-1607, 1969.

(10) Fierro-Benítez, R., J. B. Stan L. DeGroot, R. Alban, an demic cretinism in the A Ecuador. *J Clin Endocr* 228-236, 1970.

(11) Fierro-Benítez, R., M. Paredes, Endemiologic aspects of go dorean Andean region. *Rev* 387-389, 1968.

e, Tocachi, all inhabitants were
iodized oil in 1966. Two years
ren born since 1966 were injected
en of childbearing age were re-
eighboring village, La Esperanza,
eated controls. The children of
divided into two groups: Group 1
osed to adequate iodine supply
he fourth to seventh fetal month,
up 2 adequate iodine had been
the moment of conception. The
Esperanza were divided into two
orrespond chronologically with
chi. An approach to intellectual
s conducted, using the Stanford-
ence Scale as modified by the

IQ values for Tocachi Group 1
two groups from La Esperanza
69 to 73, with no significant
roup 2 from Tocachi had a mean
which was significantly greater
trol group in La Esperanza (p
ocachi Group 2, no child had an
in contrast to the other three

re defined as subjects with mental
the idiocy-imbecility level (i.e.,
tal retardation), provision of
ne supplies from the time of
ward appears to prevent endemic

CKNOWLEDGMENTS

f José Suárez, M.D., and of Edgar
Espinoza, and José Reinhart,
its, is gratefully acknowledged.
related to endemic cretinism in
sponsored by the Pan American
ation, the United States National
Health, the United States National
or Retarded Children, and the
Ministry of Ecuador.

REFERENCES

(1) Dumont, J. M., A. M. Ermans, and P. A. Bastenie. Thyroidal function in goiter endemic. IV. Hypothyroidism and endemic cretinism. *J Clin Endocrinol Metab* 23: 325-335, 1963.

(2) Choufoer, J. C., M. van Rhijn, and A. Querido. Endemic goiter in western New Guinea. II. Clinical picture, incidence and pathogenesis of endemic cretinism. *J Clin Endocrinol Metab* 25: 385-402, 1965.

(3) Fierro-Benítez, R., W. Peñafiel, L. J. DeGroot, and I. Ramírez. Endemic goiter and endemic cretinism in the Andean region. *N Engl J Med* 280: 296-302, 1969.

(4) Buttfield, I. H., and B. S. Hetzel. Endemic cretinism in eastern New Guinea: its relation to goiter and iodine deficiency. In Hetzel, B. S., and P.O.D. Pharoah, eds. *Endemic Cretinism.* Monograph Series No. 2. Institute of Human Biology, Papua, New Guinea, 1971. pp. 55-69.

(5) Delange, F., A. M. Ermans, and J. B. Stanbury. Endemic cretinism in Idjwi Island (Kivu Lake, Zaire Republic). In Stanbury, J.B., and R. L. Kroc, eds. *Human Development and the Thyroid Gland: Relation to Endemic Cretinism.* Plenum Press, New York, 1972. pp. 87-113.

(6) Ibbertson, H. K., J. M. Tait, M. Pearl, T. Lim, J. R. McKinnon, and M. B. Gill. Himalaya cretinism. In Stanbury, J. B., and R. L. Kroc, eds. *Human Development and the Thyroid Gland: Relation to Endemic Cretinism.* Plenum Press, New York, 1972. pp. 51-69.

(7) Fierro-Benítez, R., L. DeGroot, M. Paredes Suárez, and W. Peñafiel. Yodo, bocio y cretinismo endémicos en la región andina del Ecuador. *Rev Ecuat Cien Biol* 5: 15-40, 1967.

(8) Fierro-Benítez, R., I. Ramírez, E. Estrella, C. Jaramillo, C. Díaz, and J. Urresta. Iodized oil in the prevention of endemic goiter and associated defects in the Andean Region of Ecuador. I. Program design, effects on goiter prevalence, thyroid function, and iodine excretion. *Endemic Goiter.* Scientific Publication No. 193. Pan American Health Organization, Washington, D.C., 1969. pp. 306-340.

(9) Kevany, J., R. Fierro-Benítez, E. A. Pretell, and J. B. Stanbury. Prophylaxis and treatment of endemic goiter with iodized oil in rural Ecuador and Peru. *Am J Clin Nutr* 22: 1597-1607, 1969.

(10) Fierro-Benítez, R., J. B. Stanbury, A. Querido, L. DeGroot, R. Alban, and J. Córdova. Endemic cretinism in the Andean region of Ecuador. *J Clin Endocrinol Metab* 30: 228-236, 1970.

(11) Fierro-Benítez, R., M. Paredes, and W. Peñafiel. Endemiologic aspects of goiter in the Ecuadorean Andean region. *Rev Eur Endocrinol* 3: 387-389, 1968.

(12) Fierro-Benítez, R., I. Ramírez, J. Garcés, C. Jaramillo, F. Moncayo, and J. B. Stanbury. The clinical pattern of cretinism as seen in highland Ecuador. *Am J Clin Nutr* (in press).

(13) Terman, L. M., and M. A. Merrill. *Stanford-Binet Intelligence Scale.* Houghton Mifflin Company, Boston, 1962.

(14) Lagman, J. Embriología médica. Interamericana, Mexico City, 1969.

(15) Greenberg, A. H., P. Czernichow, R. C. Reba, J. Tyson, and R. M. Blizzard. Observations on the maturation of thyroid function in early fetal life. *J Clin Invest* 49: 1790-1803, 1970.

(16) Ramírez, I., R. Fierro-Benítez, E. Estrella, C. Jaramillo, C. Díaz, and J. Urresta. Iodized oil in the prevention of endemic goiter and associated defects in the Andean region of Ecuador. II. Effect on neuro-motor development and somatic growth in children before two years. *Endemic Goiter.* Scientific Publication No. 193. Pan American Health Organization, Washington, D.C., 1969. pp. 341-359.

(17) Fierro-Benítez, R., I. Ramírez, E. Estrella, A. Querido, and J. B. Stanbury. The effect of goiter prophylaxis with iodized oil on the prevention of endemic cretinism. In Fellinger, K., and R. Höfer, eds. *Further Advances in Thyroid Research.* Verlagder Wiener Medizinischen Akademia, Vienna, 1971. pp. 61-77.

(18) Ramírez, L., R. Fierro-Benítez, E. Estrella, A. Gómez, C. Jaramillo, C. Hermida, and F. Moncayo. The results of prophylaxis of endemic cretinism with iodized oil in rural Andean Ecuador. In Stanbury, J. B., and R. L. Kroc, eds. *Human Development and the Thyroid Gland: Relation to Endemic Cretinism.* Plenum Press, New York, 1972. pp. 223-237.

(19) Trowbridge, F. L. Intellectual assessment in primitive societies, with a preliminary report of a study of the effects of early iodine supplementation on intelligence. In Stanbury, J. B., and R. L. Kroc, eds. *Human Development and the Thyroid Gland: Relation to Endemic Cretinism.* Plenum Press, New York, 1972. pp. 137-149.

(20) Fierro-Benítez, R., I. Ramírez, and J. Suárez. Effect of iodine correction early in fetal life on intelligence quotient: a preliminary report. In Stanbury, J. B., and R. L. Kroc, eds. *Human Development and the Thyroid Gland: Relation to Endemic Cretinism.* Plenum Press, New York, 1972. pp. 239-247.

(21) Fierro-Benítez, R., I. Ramírez, J. Suárez, C. Jaramillo, and F. Moncayo. Effect of the chronic iodine deficiency correction on intelligence. *Isr J Med Sci* 8: 17-18, 1972.

(22) Fierro-Benítez, R. Poblaciones campesinas en regresión. Editorial Casa de la Cultura Ecuatoriana, Quito, 1971.

(23) Bonifaz, E. Origen y evolución de una hacienda

histórica: "Guachala." *Bol Acad Nac Hist Ecuad* 53: 338-350, 1970.
(*24*) Vaughan, V. C. Growth and development. In Nelson, W. E., V. C. Vaughan, and R. O. McKay, eds. *Textbook of Pediatrics.* W. B. Saunders Company, Philadelphia, 1969. pp. 15-57.
(*25*) Wilkins, L. *Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence.* C. C. Thomas, Springfield, Ill., 3d ed., 1966.
(*26*) Falkner, F. *Human Development.* W. B. Saunders Company, Philadelphia, 1966. pp. 23-26.
(*27*) Winick, M. Nutrition and mental development. *Med Clin North Am* 54: 1413-1429, 1970.
(*28*) Chase, H. P., and H. P. Martin. Undernutrition and child development. *N Engl J Med* 282: 933-939, 1970.
(*29*) Winick, M. Cellular growth during early malnutrition. *Pediatrics* 47: 969-978, 1971.
(*30*) Chase, H. P. The effects of intrauterine and postnatal undernutrition on normal brain development. *Ann NY Acad Sci* 205: 231-244, 1973.
(*31*) Cravioto, J., E. R. De Licardie, and H. G. Birch. Nutrition, growth and neurointegrative development: an experimental and ecologic study. *Pediatrics* 38: 319-372, 1966.

DISCUSSION

Dunn: I think this study is very important, because it shows that with iodine deficiency the population is not sharply divided between obvious cretins and completely normal subjects, but there seem to be many gradations between these two. Thus the whole population is at risk for some impairment of intellectual function. The economic consequences of this to a community must be enormous. Dr. Bautista has been doing a somewhat similar study in a village in Bolivia with severe iodine deficiency, and he has found mean scores on the Stanford-Binet test of approximately 70-75, as you have. Finding a culture-free test of intelligence is an old problem, and there are certainly many difficulties in comparing test scores of isolated rural populations with those of North American urban children. This does not affect the use of this test for comparative purposes within a community, but I think it is less certain that a score of 70 implies the same degree of mental deficiency in rural Ecuador that it does in urban United States. The Bolivian study will attempt to correlate the Stanford-Binet with the Bender-Gestalt, class rankings by the teachers, and probably an analysis of the subsets in the Stanford-Binet testing; and perhaps from all this Dr. Bautista will be able to tell us which measures are the most valuable for grading intelligence in these cultures.

Finally, I wonder if you can tell us whether iodine given between conception and the fourth month of gestation affects later IQ scores. This would help to pinpoint the time at which iodine is most critical.

Fierro: We did try dividing our data into several other groups and found no differences. The only improvement was in the children exposed to adequate iodine from the moment of conception.

Perinetti: The original studies in schoolchildren in Mendoza before iodization did not show a decrease in intellectual capacity, height, or weight in comparison with nonendemic regions. Perhaps the difference is that some of the other factors described by Dr. Fierro, such as malnutrition, were not present.

Pretell: In our experience in Peru, iodine deficiency may be associated with impaired intellectual capacity but does not seem to affect height or weight. This is our conclusion from data on children followed for five years after injection of iodized oil, when compared with uninjected controls from the same community. We do note growth retardation when compared with the American standards, but the growth rate is the same as that of noniodine-deficient Peruvian population from the coast. We thus would attribute this to a population standard and not to iodine deficiency or its correction. Also, from very careful anthropometric measurements, we do not find malnutrition to be a contributing factor.

IODINE DEFICIENCY

EDUARDO A. PRET
MARTHA WAN, Q.F.,[2]

Dietary deficiency of iodi
sequence, endemic goiter, con
of the most extensive prob
malnutrition in the world. In
American countries, endemic
been recognized as a sever
problem, with the most affecte
Andean region of Ecuador (*1*),
Bolivia (*4*). Nevertheless, litt
been paid to the implementa
programs for prophylaxis a
indeed, the prevalence of end
have worsened during the past d
World Health Organization h
demic goiter a relatively low pr
attention, chiefly because the
disease on development in the
born periods have not been w

The association of endemic
endemic goiter is well recogr
increases the importance of
because it has adverse effects
ment of the community. The
rate among cretins may be qu
who survive into adulthood
degrees of physical or mental in
severely limits their value to th
to the community.

Querido has strongly advar
thesis that the prevalence of cre
to the severity of iodine deficie

[1]This work was supported in par
Health and Social Welfare Fund of P
and USPHS grants, AM-12748, AM-
14039.
[2]Altitude Research Institute, C
University, Lima, Peru.
[3]Endocrine Section, Departmer
University of Pennsylvania, School o
delphia, Pennsylvania.
[4]Unit of Experimental Medicine
Nutrition and Food Science, Massac
of Technology, Cambridge, Massachus