

# Effects on school children of prophylaxis of mothers with iodized oil in an area of iodine deficiency<sup>1,2</sup>

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**ABSTRACT.** The results of tests of intellectual and psychomotor performance and school performance in a group of school children from a rural impoverished and iodine deficient Andean community whose mothers received injections of iodinated oil prior to the end of the first trimester of pregnancy have been compared with results in children from a neighboring comparable community whose mothers had received no iodinated oil. Subjects between ages 8 and 15 were studied. Statistically significant differences were not observed between the two groups in tests of intellectual function, but children of mothers who had received iodinated oil performed better on tests of psychomotor maturation. The group whose mothers had received oil performed distinctly better when assessed in terms of school drop-out rates, grades achieved, grades repeated, and in overall performance as judged by teacher notes in school records. Performance of both groups on standard tests of intellectual and psychomotor function was lower than standard scores. This may be a result of social and cultural deprivation, the general malnutrition prevailing in the region or other unidentified factors. The improved scoring and school performance exhibited by the children of mothers who received iodinated oil underlines the importance of prophylaxis with iodine in iodine deficient regions as one important contributor to community development.

## INTRODUCTION

An inventory of the total population of ten rural communities of the Ecuadorean Andes affected by goiter was made in 1962 (1, 2). Chronic iodine deficiency, protein-calorie malnutrition, isolation and cultural deprivation prevailed in these communities. In addition to overt cretinism, mental subnormality appeared to afflict a large fraction of the population. Two of these communities were chosen for study: Tocachi and La Esperanza. These were neighboring villages, similar in altitude, isolation, ethnic make-up, iodine deficiency and socioeconomic conditions. Prevalence of goiter and cretinism were similar (3, 4).

A program of correction of chronic iodine deficiency by intramuscular administration of iodized oil (Ethiodol) was started in March, 1966. The total population of

Tocachi was treated, La Esperanza serving as control. Those born after the program was started were examined at the time of birth and at key stages of their development. Physical growth and neuromotor development were measured. Women of childbearing age and children born in Tocachi were reinjected or injected in 1970, 1974 and 1978, after it was shown that the dose of Ethiodol used maintained the urinary excretion of iodine above 50 micrograms per gram of creatinine for 4-5 years. The results up to 1973 may be summarized as follows: 1) Goiter was prevented in children born in the treated population; 2) gross motor function showed a net improvement in the children of the treated mothers, the difference with children of untreated mothers being significant; 3) deafness-related mutism did not occur in children of treated mothers; 4) among the children of untreated mothers there were instances of definite retardation in all four major areas of neuromotor development (personal-social, reflex maturation, linguistic and motor areas). These children were diagnosed as endemic cretins (3-9).

Results of correction of chronic iodine deficiency on intellectual capacity were studied in 1973, when the children born under the program were up to seven years old. These showed generally poor performance in children of both treated and non-treated mothers. When the distribution of IQ scores (Stanford-Binet test)

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was charted, the curve of the untreated children was skewed in the direction of mental deficiency, while the curve of the treated children showed a clear tendency toward normality. Severe mental deficiency (IQ > 50) did not appear in children born of mothers treated with iodized oil before conception or before the first three months of pregnancy. In children of untreated mothers the spectrum of intellectual capacity was wide, covering practically all mental categories (10-13). We adopted the term *endemic mental deficiency* for all categories of mental retardation found in the communities, realizing that *all* of these defective children were not attributable to iodine deficiency.

Since 1969 there has existed mandatory iodization of salt for human consumption, but the 1978 (14) and the 1981 (15) surveys disclosed that the prevalence of goiter in school children had not significantly diminished (except in Tocachi). Urinary excretion of iodine in the great majority of the rural population remained under 50 micrograms per gram of creatinine.

In October 1981, we began the present study of the effects of correction of iodine deficiency on intellectual development. A large number of the children born in the two communities after 1966 had entered school. It was possible, therefore to study their school performance. Age six to seven is a milestone in a child's mental development (16, 17). The psychological life of the child, both in relation to intelligence and to affective life, social relations, and individual activity is observed in the appearance of new forms of organization that complete the structures which were being formed during earlier periods of development. In the intellectual area, logical thinking appears during the early school years. The principle of logic, or causality constitutes a system of relations that permit the coordination of diverse personal view points, and the coordination of perceptions and intuitions (16). The presence of concrete operations, both logical-arithmetic and spatial-temporal, in the child's thinking, and its governance by a set of common rules, characterize the unfolding mental structure and permits the child to respond to the demands of the educational system (18, 19). The development of thought is stimulated to an undefined degree by the formal schooling process and by the acquisition of specific skills such as the ability to read and write. By the end of schooling the child has learned to generalize and to elaborate abstract constructions, and this opens him to a more sophisticated interpretation of reality. In the domain of the affective life, systems of social and individual coordination become organized in the school child, leading to the appearance of social integration. The development of rational thought and behavior, autonomy, honesty, will-power and responsibility are important aspects in the evolving affective life of the school child (20).

A normal child adapts rapidly to school and responds to the instructional system because he has the intellectu-

al tools necessary for learning. Results of intelligence tests have always correlated with school success (21). A study, therefore, of school performance in subjects born under a program of correction of iodine deficiency should disclose the long-term effects of such correction in relation to its most important aspect, the prevention of mental disabilities which leave the child at a disadvantage. It also seemed reasonable to complement the school performance evaluation with that based in formal tests of intelligence. Although we were well aware that cultural differences introduce changes in test results (22), and that those tests that we used had not proved to be entirely culture-free, we realized that western tests often work with other cultural groups when adapted to increase their intelligibility and acceptability (23).

## MATERIALS AND METHODS

School performance of children born under the program from October 1966 to October 1973 were studied beginning in October 1981, both in Tocachi (treated population) and in La Esperanza (non-treated population), i.e. in subjects who by 1981 were 8 to 15 years old. All subjects in Tocachi had been born to mothers treated before conception, or during the first three months of pregnancy. Elementary school in the communities takes six years, and children start between five and seven years of age. The study of school performance was conducted only on those children who had stayed in school at least a full year and had started a new year, even if they had not completed the second year.

The sources used in studying school performance were: 1) the School Register, a book maintained by teachers; 2) the Annual Student Report, which the pupil receives at the end of the school year; 3) interviews with teachers and parents; this information was recorded in the "School History" of each child, including the age at which he started school; 4) marks at the end of each grade in the four basic areas of elementary school, including reading, writing, mathematics and natural science; 5) grades passed or repeated and cause for failure; 6) drop-outs and transfers, and 7) any special remarks on the child's behavior and performance.

Six-hundred and fifty children were born under the program from October 1966 until October 1973, of whom 239 were in the treated population and 411 in the non-treated population. It was possible to study school performance in 421 children (64%), of whom 128 (59%) were in the treated group and 293 (71%) in the untreated population. These were children who were still in school, or had finished or abandoned school. The missing children were from death before entering school, failure to enter school, some who did not stay in school for a full year, some who had moved and could not be traced, some with incomplete school registers, and

some for whom there were inconsistencies between school registers and student reports.

Size of thyroids of all subjects was assessed by skilled examiners according to the classification of the Pan American Health Organization (24).

A set of tests was administered to those students whose school performance was studied. Children from the untreated group were pair-matched by age and sex, with one for each child from the treated group. When more than one subject was available to match a subject from the treated group, random selection was employed. All were volunteers. Although frequently several tests were done on the same subject, in no case were more than two done on the same person in a single session. This part of the study was done by a psychometrist with wide experience in field work among Andean rural communities. The tests used follow.

#### *Terman-Merrill*

This version of the Stanford-Binet Scale (25), modified by Navas for Ecuadorean children (26), is an intelligence test requiring verbal, numerical and spatial ability. The Navas adaptation omits some purely verbal items and others that rely too much on memory. The test correlates with school performance in 70% of cases. In children from the urban center, Quito, the IQ distribution was similar to that reported by Terman and Merrill. The test was applied to 113 children from the untreated community and 41 from the treated group, all aged 8 to 12.

#### *Wechsler*

This test was also a version modified by Navas for local use (27, 28). The Wechsler test is based on the concept that intelligence is the "capacity to act in a purposeful way, to exert pressure rationally and to try to cope with one's environment efficiently". The test requires attention, immediate memory, imagination, verbal, numerical and spatial ability, visual perceptive ability, ability to concentrate, inductive reasoning, global perception of elements, aptitude to understand a situation as a whole, ability to analyze and synthesize, and speed and accuracy in manual performance. The resulting IQ is an indicator of general cognitive aptitude. We applied it to 55 subjects from the untreated group and to 53 from the treated group. All were older than 12.

#### *Goodenough*

This test of child intelligence is based on the drawing of the figure of a man (29). It is based on the hypothesis that the child "draws based more on what he knows than on what he sees". It attempts to measure general intelligence of children up to age 13. Goodenough interpreted spontaneous child drawing as an objective expression of higher physiological processes. The child when drawing "does not perform an esthetic process but an intellectual task. He does not produce an

expression of artistic ability but one of conceptual reportory". She pointed out that graphic activity tends to integrate along a gradual process of psychological maturation. The test is widely used regardless of cultural roots or cultural developmental levels. In these studies it was used on 168 children from the untreated community and on 94 from the treated community, and on subjects aged 8 to 13.

#### *Goddard*

The child fits ten geometrical figures into their appropriate places as rapidly as possible, using one or both hands (30). The test may be used both in children and adults; since language is not used it may be used on those with hearing disorders and those with mental retardation. It assesses psychomotor development, manual ability, visual motor coordination and the ability to recognize shapes and meanings. It was used with 170 children from the untreated community and 94 from the treated one.

#### *Bender*

In this visual-motor test the examinee copies nine gestalt designs (31). Through analysis of the copies the examiner can evaluate the manner in which the subject has structured the perceptual stimuli. It can be applied to children and adults, literate or illiterate, and those with language problems. It is founded on the theory of form, and is a visual-motor one since the subject draws with a model in sight. According to Bender it addresses visual perception, motor-manual ability, memory, spatial concepts and ability to organize and represent. It permits the diagnosis of organic problems of the brain, mental retardation, aphasias, and the level of maturation. It was applied to 141 persons from the untreated community and 42 from the treated one, and on subjects aged 8 to 15.

#### *Raven*

This progressive matrices test is based on the assumption that "intelligence is determined by a large number of specialized factors—one for each function, by a limited number of group factors (that intervene in a number of functions), and by a general factor (common to all functions)" (32, 33). The test is non verbal, graphic, multiple choice, and is an endeavor to measure "the intellectual ability necessary to compare shapes, and to reason by analogy with independence of acquired knowledge". In a study conducted in Ecuadorian schools this test was found useful "to classify with economy and simplicity of instruments the intellectual ability of large groups of school children" (34). We applied it to 167 children from the untreated community and to 94 from the treated one, ages 8 to 15.

Body weight and standing height of all subjects of this study were measured, and the data compared with those obtained in the same villages before the prophylaxis program was begun. In 72 subjects from the un-

treated community and in 31 from the treated region the urinary excretion of iodine was measured and expressed in ug/gm creatinine, following standard methods (35, 36). All subjects for iodine measurements were older than 10 and were chosen because the heights and weights were similar in the two groups.

A quarterly determination was made of the iodine content of the four types of salt sold in the two communities during 1981-1982. The more expensive ones were labeled "iodized salt" while the last was rock salt. During the same period a survey was made among 20% of randomly chosen families in the two communities in order to determine the kind of salt used.

In some cases radioimmunoassay for TSH was done on dried filter paper spots (Phadebas Dry Spot TSH kindly provided by Pharmacia Diagnostics). Tests were performed in duplicate samples on 3.0 mm discs.

## RESULTS

### Prevalence of goiter

Stage 1 goiter (thyroid palpable and visible only when the neck is fully extended) was found in 21% of the study subjects in the untreated community and in 2% in the other. Nodular goiter was found in 7% of subjects in the untreated group.

### Urinary excretion of iodine

Excretion was significantly higher ( $P > 0.001$ ) in the treated than in the untreated community (Table 1). More than 50% of those from the untreated group had values under 50 ug/gm creatinine.

### Iodine content of salt

"Iodized salt" (3 brands) had mean values for the quarterly determinations of 15, 5 and 2 ug/gm, while there was no iodine detected in the rock salt. The family survey showed that 70% of the families used one of the brands of "iodized salt", 14% used it occasionally, 12% not at all, and 4% did not respond.

### Weight and height of subjects

There were no significant differences in these parameters between the two groups. There were no differences between the two groups when data were obtained from the two communities on the same subjects

Table 1 - Number, mean value and range, SD and "Z" Test value of p, of urinary excretion of iodine ( $\mu\text{g/g}$  creatinine) in treated and untreated children older than 10 yr.

Group	Number	Mean value (range)	SD	"Z" Test value of p
Treated children	31	207.2 (34-483)	132.2	$p < 0.001$
Nontreated children	72	116.0 (20-377)	92.5	

before the program was begun several years earlier (6, 13, 37).

### School performance

There was no difference between the treated and untreated children with respect to the age at which they started school. The average age at which they entered was that usual for Ecuadorean children. Those from the treated group began at 6.67 years, and from the untreated group 6.69 years. The range was larger than that for urban Ecuadorean children, being 5.3 to 8.8 years among the treated children and 5.3 to 8.9 for the untreated group.

At the beginning of this study most of the subjects from the treated group were in the fifth and sixth grades, while most of those from the untreated group were in the fourth and fifth grades (i.e. one year's difference) (Table 2). There was a higher percentage of those from the treated group who had finished elementary school and were in high school. Evidently this was not due to socioeconomic reasons since the percentage of children taken out of school for family problems or for work needs was similar in both groups. The percentage of children from the untreated group taken from school for mental insufficiency was twice than from the treated group. Three children from the untreated group were removed from school because of obvious mental retardation in two and impaired hearing in one. Most of the children who withdrew from school did so at two times: at the end of the first grade, when it became obvious that they could not continue because of extremely poor performance, and at the end of the fourth grade, again for poor performance. In the opinion of the teachers these children were unable to progress to upper grades, where higher degrees of abstraction and

Table 2 - Situation of the treated and untreated children when the study started (October, 1981).

	Treated	Untreated
<i>School:</i>		
1st. Grade	0.0%	0.6%
2nd. Grade	3.0%	1.7
3rd. Grade	7.8	12.6
4rd. Grade	11.7	17.0
5th. Grade	26.5	15.6
6th. Grade	17.2	10.2
Have completed the School but did not continue their studies.	10.9	16.0
Are in the High School	6.2	2.7
Left School for socio-economic reasons	10.9	9.8
Left School for incapacity (very low performance).	5.4	13.3

generalization are needed. Seven children (5.4%) from the treated group and 39 (13.9%) from the control group were removed from school for mental deficiency. In 6 of the children from the treated group and in 28 from the untreated group we were able to determine the plasma TSH levels. All except 3 from the untreated group had values below 7 uU/ml blood. The elevated values were 10, 14 and 30. The parents did not consent to other measurements.

#### *Performance of children who had not failed any grade*

The indicators used were grades received in reading, writing, mathematics and natural science during each year the student stayed in school. Among the treated group 58% had failed no grade, while 36% from the control had not failed a grade. A higher percentage of the children from the treated group received good marks (16% vs. 9%). Analysis of grades showed that performance was especially deficient in reading and writing until the fourth grade, and in all four areas in the upper grades.

#### *Children who had failed at least one grade*

The number of children (80%) in this category came from the untreated group more frequently than from those whose mothers had been treated (64%) (Table 3). The difference was largely due to performance in the first grade, when 20% of the treated group had to repeat, while 45% of the untreated group were repeaters. Performance in these children was especially low in reading and writing, and above all in mathematics. It appeared that the reading and writing problems could not be assigned to dyslexia or dysgraphia, but rather to a global retardation indicated by low levels of understanding and retention. The School Register at this level noted that some children could not learn to read. A diagnosis of dyslexia could be made on only two of the 128 children, both from the treated group.

Grade repetition was evident in both groups, but was higher in the children from untreated mothers (Table 4). Among the treated children 26% showed one year difference from the grade they should have been in, compared to 46% of the untreated children. Two year differences were similar in the two groups.

#### *Causes for failure*

In the teacher's opinions the children who did poorly or failed did not "respond to stimuli", "were apathetic" or "inhibited". Interviews with the children readily distinguished between apathy and laziness. In the apathetic children there was something beyond laziness: lack of knowledge and incapacity were related to the child's memory. School Register notes frequently recorded that "the child does not remember", or "forgets everything". Three children from the treated group and nine from the untreated group who were starting the third grade had practically forgotten how to read and write. There appeared to be no differences between boys and girls in all aspects reported here.

Table 3 - Percentage of the treated and untreated children who repeated a given grade.

Grade	Treated	Untreated
1st	20%	45%
2nd	13	14
3rd	18	11
4th	9	7
5th	3	2
6th	1	1

Table 4 - Times a grade was repeated by treated and untreated children:

	Treated	Untreated
One Time	26%	46%
Two Times	12	14
Three Times	4	3
Four Times	-	1

Table 5 - Number, mean IQ scores and range, SD and "Z" Test\* value of p, of the treated and untreated children aged 8-12 years, tested with the Terman-Merrill Test (25) modified by Navas (26).

Group	Number	IQ mean value (range)	SD	"Z" Test value of p
Treated children	41	90.73 (64-109)	10.29	NS
Untreated children	113	88.85 (50-108)	10.68	

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

Table 6 - Number, mean IQ scores and range, SD and "Z" Test value of p, of the treated and untreated children, all older than 12 years, tested with the Weschler Test (27) modified by Navas (28).

Group	Number	IQ mean value (range)	SD	"Z" Test value of p
Treated children	53	92.41 (71-126)	13.22	NS
Untreated children	55	89.58 (64-111)	10.85	

Table 7 - Number, mean IQ scores and range, SD and "Z" Test value of p, of the treated and untreated children, aged 8-13 years, tested with the Goodenough Test (29).

Group	Number	IQ mean value (range)	SD	"Z" Test value of p
Treated children	94	88.52 (51-115)	12.73	NS
Untreated children	168	88.31 (48-117)	13.13	

Table 8 - Number, mean IQ scores and range, SD and "Z" Test value of p, of the treated and untreated children aged 8-15 years, tested with the Goddard test (30).

Group	Number	IQ mean value (range)	SD	"Z" Test value of p
Treated children	94	91.96 (60-113)	12.23	$p < 0.002$
Untreated children	170	85.31 (50-113)	13.55	

Table 9 - Results obtained with the Bender Gestalt Test (31) in 42 treated and 141 untreated children aged 8-15 years.

Bender classification	Treated children %	Untreated children %
Normal (N)	44.6	30.4
Normal Inferior (NI)	29.7	27.6
Signs of Immaturity (SI)	19.1	29.7
Abnormal (A)	6.5	12.0

Table 10 - Results obtained with the Raven test (32, 33) in 94 treated and 167 untreated children aged 8-15 years.

Percentile	Treated children %	Untreated children %
1	6.3	1.7
5	21.2	26.9
10	43.6	26.3
15	—	0.5
25	14.8	25.1
50	13.8	18.5
75	—	0.5

Performance on Tests

Terman-Merrill-Navas test

This test of general intellectual aptitude disclosed that the IQ's of children from the treated group did not reach a significant difference from the control group (Table 5). In both groups the average and most scores were well to the left of the established distribution curve. 14.6% of the children of treated mothers and 18.% of the control group had deficient performances as compared to established standards. This deficiency appeared in the following aspects: information, comprehension, analogies and differences, reasoning, abstraction, recall and immediate memory, and vocabulary.

Wechsler-Navas test

The IQ's as measured by this test of intelligence did not reach a significant difference between the groups (Table 6). Both the average and most scores in both groups were also to the left of the established curve for a normal population. 15.1% of children from the treated group and 21.8% of the control group showed deficient performances. The deficiency related to visual-perceptual aptitude, immediate memory, attention span, ability to concentrate, inductive reasoning, ability to grasp a situation as a whole, and learning speed.

Goodenough test

There were no differences between groups with this test of intelligence (Table 7). Averages and most scores of both groups were below those of the standard curve. 23.4% from the treated group and 25.4% of the untreated group showed deficient performance. In addition to retardation indicated by omission of elements of the drawn figures, the drawings showed failure in motor coordination and speed of movement.

Goddard test

There was a significant difference between the groups in performance on this test of psychomotor development (Table 8). Among the children of untreated children 28.8% showed deficient performance, whereas among the treated group 11.7% were deficient. The deficiencies had to do with manual skill, visual-motor coordination, speed of movement, recognition of shapes and background-figure discrimination.

Bender test

Results of this test, which primarily evaluated integration of the visual-motor items, showed that 25.6% of the treated group had lack of maturity (SI) or were abnormal (A), whereas 41.7% of the untreated group were found to be immature or abnormal (Table 9). The children of treated mothers presented a normal frequency distribution, whereas children of the untreated group showed almost the same number of children in the normal, normal inferior, and the SI group. In the untreated community in an earlier study (38) 17% of apparently normal adults showed clear signs of neurological deficit in visual motor perception.

*Raven test*

The results of this test (Table 10) did not correlate with those of the three other tests of intelligence: Less than a fifth of the subjects reached the 50th percentile, equivalent to an average level of intelligence, and the scores of the treated group were poorer than those of the untreated group. According to Bernstein (33) this test is not one for evaluating mental deficiency.

## DISCUSSION

This study is not one of cretinism or of cretinoid individuals, since it was conducted on children who were judged initially by their parents and the teachers as suitable for entry into school. It is an investigation of school performance and of the results of tests of psychomotor function and intellectual maturation in a group of school children born of mothers who had received iodinated oil by injection prior to the completion of the first trimester of pregnancy with a control group of children from a similar and neighboring village whose mothers had not been given iodinated oil. It is evident that iodine had become available to some of the children in the control group. The reasons for this was the penetration of iodized salt into the market place and an intervening program of administration of iodinated oil in the control community which through environmental recycling made iodine more available to the children of the communities.

Most subjects in both groups developed under conditions of protein-calorie malnutrition and cultural deprivation, but the lack of differences in height and weight between the two groups indicates that general nutrition was not the cause of the differences in school and test performances. Nevertheless, malnutrition is well established as a cause of poor development (39, 40). Malnutrition, isolation, and a hostile and poor social environment probably contributed to the general low performance on the various tests of intellectual and neuromotor maturation.

The instruments used to gauge school performance in the two groups of children showed that while there was a significant percentage of subjects with a net deficient performance, the percentage was greater in the children born of mothers who did not receive iodinated oil. The deficiencies were most apparent in reading, writing, and mathematics, and indicated a generalized low level of comprehension of what they read or heard, low levels of abstraction and generalization, deficient vocabulary, inattention, motor inability and impaired memory.

The results of intelligence testing correlated well with school performance, confirming that in both groups there were significant percentages of mentally subnormal subjects. Although these intelligence tests are far from perfect, they are the most reliable instruments that can be used for this purpose. Educators and psy-

chologists use them extensively and with enough success to justify their use in school children (21). Navas (34) found in Ecuadorean school children that there was a good correlation between the results obtained with the Terman-Merrill, Wechsler and Goodenough tests and school performance, and we found that these tests did not distinguish between the treated and the untreated groups. It may be assumed that the subnormality measured by these tests was caused by factors in addition to iodine deficiency.

Since in both the Goddard test (which measures psychomotor development) and in the Bender test (which measures integration of functions on the basis of visual-motor items) the children in the untreated group scored significantly lower, we may assume that thyroid deficiency caused by iodine deficiency affects the maturation of those processes that make possible maturation and integration of different functions of the nervous system, such as psychomotor function. Significant differences between iodine deficient and sufficient populations have been found in regard to a number of perceptual and neuromotor abilities in Spain and in Central Java (41).

These studies do not distinguish definitively between two of the possible interpretations of the differences noted between the two groups. The lower level of iodine intake (indicated by the fact that more than 50% of the children of the control group had urinary levels of iodine below 50 ug/gm creatinine) raises the possibility that differences in ambient thyroid function may have been responsible. Alternatively, the differences may have arisen from differing levels of neural maturation between the two groups. While we favor the latter interpretation, we cannot rule out the other.

While the studies reported here fail to show significant differences between school children whose mothers received iodine prior to the end of the first trimester of pregnancy and those whose mothers did not in the results of several tests of intellectual function, they did show distinct differences in maturation of psychomotor function between the two groups. More importantly in our opinion, there were also pronounced operational differences between the two groups when measured in terms of a number of indices of performance in school.

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