# THE RELATIONSHIP OF A LOW-IODINE AND HIGH-FLUORIDE ENVIRONMENT TO SUBCLINICAL CRETINISM IN XINJIANG

**Lin Fa-Fu, Aihaiti, Zhao Hong-Xin, Lin Jin, Jiang Ji-Yong, Maimaiti, and Aiken. Xinjiang Institute for Endemic Disease Control and Research; Office of Leading Group for Endemic Disease Control of Hetian Prefectural Committee of the Communist Party of China; and County Health and Epidemic Prevention Station, Yutian, Xinjiang.**

Cretinism in iodine-deficiency areas is well known, yet the milder forms of somatic and psychomotor maldevelopment and thyroid dysfunction caused by iodine deficiency may be more difficult to detect. DeQuervain, in 1936, called this milder form "semi-cretinism," while in 1980 Laggasse used the term "cretinoidism." It was formally named "subclinical endemic cretinism" at a symposium on subclinical cretinism held in Xinzhou, Shanxi province in 1985. Currently, attention is being focused on these disorders in China and abroad. The Hetian prefecture in Xinjiang has reportedly been one of the Asian areas most severely affected by iodine deficiency disorders (IDD). During the period 1987-1989, we made a systematic survey of subclinical endemic cretinism in this district under a UNICEF aid Project.

## Materials and Methods

**General conditions and selection of affected areas** - The entire region of Xinjiang in central Eurasia is affected by iodine deficiency. The study area, located between the southern border of Tarim basin and the northern slope of Kunlun Mountains, is arid with sandy soil and an annual precipitation less than 50 mm. The cultivated alluvial plain extends from south to north with a steepening gradient. The geographical distributions of endemic goiter and endemic fluorosis are characterized by marked vertical zones. The inhabitants are of lower socioeconomic status, with an annual mean income of about 200 yuan (RMB) per person.

**Area with high fluoride and low iodine levels** (Area A) - In the township Xinyuan in the lower reaches of Kliya river in the county of Yutian, north of the highway, we examined 250 schoolchildren, aged 7-14 years. The goiter prevalence was 91% and dental fluorosis 20.80%. The average level of iodine in drinking water was 5.21 μg/l, and that of fluoride 0.88 mg/l.

**Area with low iodine level** (area B) - In the townships of Langan and Jiayi in the alluvial plain before the mountains and to the south of the highway, we examined 256 schoolchildren, aged 7-14 years. The goiter prevalence was 82% and dental fluorosis of 16.00%. The average water iodine level was 0.96 μg/l and that of fluoride 0.34 mg/l.

**Control area with iodine supplementation** (Area C) - In the suburbs of Hetian where the nationalities, habits, customs, and income were basically similar and where iodine supplementation in the form of iodized salt or oil has been implemented since 1982, we examined 243 schoolchildren aged 7-14 years.

## Methods of Examination

**Intelligence test** - We used the Combined Raven's Test for Rural China (CRT-RC). It is culturally fair, non-linguistic, and particularly suitable for intelligence screening in minorities. According to the scale, an IQ of 50-69 means mild mental retardation. *Hearing* was tested with different frequencies by electroaudiometry with MST Audiometer (Nagashima Medical Instruments, Co., Ltd.). *Psychiatric-psychological function* was tested by the reaction time tester type XZ-I, knock tester type QJ-I and action stability tester type WD-Z (Chengde Medical Apparatus and Instruments Factory), with Ding Zhi-Min's normal values of psychomotilities as references (2). *Bone age* was estimated from right palmar carpal roentgenograms by the method of Li Guo-Zhen (3). *Thyroid $^{131}I$ uptake in 24 hours* was determined using automatic scaler type 126 and GM tube. *Thyroid hormones* were measured with kits provided by the Beijing Institute of Atomic Energy.

**Methods of epidemiological study** - We randomly selected a class of students in each affected area and examined for endemic goiter, endemic fluorosis, body height, weight, and intelligence. Using random stratified sampling method, we examined 10-12 students for hearing, the four psychomotilities, bone age, thyroid I131 uptake and thyroid hormone. The data obtained were analyzed by variance and multivariate stepwise regression with IBM-XT electronic computer.

## Results and Analyses

**Somatic development of children aged 7-14 in iodine-deficient areas** - The values for weight/height X 100% of 295 children from the iodine-deficient areas showed a retardation of 1 to 1.5 years compared to those of 1,632 iodine supplemented children from suburb of Urumqi ($p < 0.01$). In area A, 29% showed detectable bone retardation, compared with 13% in area B and 6% in control area C.

Table 1 shows comparative data for the three areas. Both iodine deficient areas (A and B) differed from the control area C by having lower IQ's, higher hearing threshold, increased $^{131}I$ uptake, higher TSH, and lower urinary iodine. Area A (high fluoride, low iodine) differed from area B (normal fluoride, low iodine) by having lower mean IQ, higher TSH, slightly higher $^{131}I$ uptake, and higher urinary iodine.

**Relationships between IQ of children in iodine-deficient areas and parameters of somatic development, psychomotility and thyroid function** - The relationships of IQs of 130 patients with complete data to 15 factors were studied by correlation analysis and stepwise regression analysis. Factors closely related to IQ were, in order, age, frequency of knock, weight/height X 100% and TSH.

**Abnormality rates of various parameters of feebleminded children, aged 7-14** - In children with IQ in the range of 50-69, indices of all parameters were beyond the normal range. The abnormality rates of different parameters were, in turn, 74% for ratio of weight/height/age, 59% for TSH, 61% for thyroid $I^{131}$ uptake, 60% for frequency of mistake, 47% for frequency of knock, and 35% for hearing. In terms of accessory diagnostic conditions for subclinical cretinism (4), those who met one item of the conditions accounted for 69% and those who met two items made up 56%.

## Discussion

One hundred and four children with mental retardation were detected in all. Area A had 25%, area B 16%, and area C 8%. The significant differences in IQ among these regions suggests that fluoride can exacerbate central nervous lesions and somatic developmental disturbance caused by iodine deficiency. This may be in keeping with fluoride's known ability to cause degenerative changes in central nervous system cells and to inhibit the activities of many enzymes, including choline enzymes, causing disturbance of the nerve impulse (5). We found significant differences among the three areas, indicating that lack of iodine in children results in disturbance of the process of growth and ossification and that high fluoride intake can further disturb bone development (6,7). Also, the auditory threshold was significantly different among the three areas, with severe loss of hearing in high fluoride and low iodine areas. Severe iodine deficiency in early fetal life has adverse effects on the development and differentiation of the acoustic organ, and we suggest that high fluoride intake may also promote hearing loss.

In this study, we found that 69% of the children with mental retardation had elevated TSH levels. IQ and TSH were negatively correlated. Many investigators regard an elevated TSH in the presence of normal $T_4$ and $T_3$ levels as evidence for hypothyroidism that is subclinical but that can still affect the development of brain and cerebral function to some degree (6). Reverse $T_3$ ($rT_3$) is formed from $T_4$ by 3- deiodination in peripheral tissue. The balance of active $T_3$ and inactive $rT_3$ in the serum reflects thyroid hormone economy. In high fluoride and low iodine areas, the $rT_3$ value was 58 ng/dl (the normal value, 21 ng/dl), and the ratio of $rT_3/T_3$ was 2.91, significantly low. In areas of low iodine the $rT_3$ value was 32 ng/dl, and the ratio of $rT_3/T_3$ was 5.8. It is possible that excess fluoride ion affects normal deiodination.

We detected 104 cases with mental retardation among 769 schoolchildren, aged 7-14, in different affected areas. Some 69% of our cases with mental retardation had one or more items of the accessory conditions recommended for the diagnosis of subclinical cretinism by the National Conference on Subclinical Cretinism held in Xinzhou (4). According to the cautious suggestion of Qian Qi-Dong that the diagnosis should require two or more of the accessory conditions, 56% of our cases could still be diagnosed as having subclinical cretinism.

Currently, in the vast remote areas of South Xinjiang the control of IDD with iodized salt has not yet been generally implemented and the prevalence of subclinical cretinism is still high. This situation is a great obstacle to the child health, agricultural development, and economic prosperity of minority nationalities in South Xinjiang and necessitates prompt implementation of iodine supplementation to control subclinical cretinism.


## Summary

We studied a total of 769 schoolchildren of 7-14 years in three areas, characterized by intakes of (A) low iodine, high fluoride; (B) low iodine, normal fluoride; and (C) iodine supplemented, normal fluoride. Results for the following parameters for areas A, B, and C, respectively were: (a) average IQ: 71, 77, 96; (b) average auditory threshold (in dB): 24, 20, 16; (c) bone age retardation (%): 28, 13, 4; (d) thyroid $^{131}I$ uptake (%): 60, 50, 24; and (e) serum TSH (μU/ml): 21, 11, 6. Statistically significant differences existed between these areas, suggesting that a low iodine intake coupled with high fluoride intake exacerbates the central nervous lesions and the somatic developmental disturbance of iodine deficiency. The detection rate of subclinical endemic cretinism in children with mental retardation was 69%, and the total attack rate of subclinical endemic cretinism 9%.


## References


1. Ma Xin-Yuan, et al 1987 The study of subclinical endemic cretinism in Fujian province. Proceedings of the 3rd National Conference on Endemic Goitre and Endemic Cretinism. Chinese Centre for Endemic Disease Control and Research, pp 120-125.
2. Ding Zhi-Min 1987 Use of psychomotility function test and exploration of its normal values. Chinese J of Control of Endemic Diseases 3:18-20.
3. Li Guo-Zhen, et al 1979 A study of the development of bone: II Percentage estimation of bone age. Chinese J Rad 13:19-23.
4. Li Jian-Qun, et al 1987 A Practical Handbook of Prophylaxis and Treatment of Endemic Goitre and Endemic Cretinism. Chinese Environmental Science Publishing House, 1st edition, pp 64-69.
5. Ren Da-Li 1989 An investigation of intelligence development of children aged 8-14 years in high-fluoride and low-iodine areas. Chinese J of Control of Endemic Diseases 4:251.
6. Liu Cheng-Shan, et al 1987 Studies on diagnostic criteria for subclinical cretinism. Proceedings of the 3rd National Conference on Endemic Goitre and Endemic Cretinism. Chinese Centre for Endemic Disease Control and Research, pp 142-147.
7. Zhang Ying-Xiu 1989 Effect of fluoride on the growth development of children. Chinese J Endemiology 4:240.
8. Qian Qi-Dong 1987 Subclinical endemic cretinism. Chinese J Endemiology 6:4-9.


**Table 1. Comparative data on three areas, with high fluoride low iodine (Area A), low iodine (Area B), and control with iodine supplements (Area C).**

| | Area A | Area B | | Area C |
|---|---|---|---|---|
| | | Jiayi | Langan | |
| IQ | 71[2,3] | 79[2] | 77[2] | 96 |
| Hearing threshold | 25[2] | 20[1] | — | 16 |
| Reaction time (msec) | 827 | 1142 | 858 | 813 |
| Mistake frequency | 3.5 | 3.5 | 2.9 | 3.2 |
| Knock frequency | 70[4] | 60[2,6] | 71 | 75 |
| Action stability | 0.21 | — | 0.28 | 0.25 |
| Grip strength ratio | 0.85 | 0.88 | 0.89 | 0.88 |
| $^{131}I$ uptake (%) | 59[2,3] | 50[2,5] | 56[2] | 24 |
| TSH (μU/ml) | 21[2,4] | 11[2,6] | 16[2] | 6 |
| T4 (μg/dl) | 9 | 11 | 10 | 12 |
| T3 (ng/dl) | 169 | 200 | 186 | 199 |
| rT3 (ng/dl) | 58[4] | — | 32[2] | 55 |
| Urine I (μg/g creat) | 79[2] | 64[2] | 53[2] | 97 |
| Urine F (mg/L) | 2.56[1] | 1.61[1] | 1.34[1] | 1.6 |

[1]Difference from C significance $p < 0.05$
[2]Difference from C significance $p < 0.01$
[3]Difference from B significance $p < 0.05$
[4]Difference from B significance $p < 0.01$
[5]Difference between Jiayi and Langan $p < 0.05$
[6]Difference between Jiayi and Langan $p < 0.01$

# THE SHORT-TERM EFFECTS OF THE IODINE SLOW RELEASE DEVICE IN PREVENTING AND CONTROLLING ENDEMIC GOITER


**Lin Fa-fu, Lin Jin, Sun Yu-zhen, Shaniya, Wang Sheng-ling, Jiang Ji-yong, and Gao Jian-min, Xinjiang Institute for Endemic Disease Control and Research and Office of Endemic Disease Control in Tulufan District, Xinjiang.**



Every family of the Xinjiang minority in the People's Republic of China uses a salt jug for cooking that contains the local rock or beach salt in solution and does not buy or use iodized salt. We designed and produced the Iodine Slow Release Device (ISRD) and put it into salt jugs of families in the Township of Putaogou in Tulufan District, Xinjiang. We calculated that each member of a family consumed about 31 ml salt solution containing 226 μg iodine per day. Six months later the average iodine concentration in the salt jug solution was 7.9 μg/l. The prevalence of endemic goiter decreased from 61% to 36% ($x^2 = 81.5$, $p < 0.001$), the thyroid $^{131}I$ uptake at 24 hours decreased from 50% to 32, the urinary iodine level increased from the background level 84.34 μg/gm creatinine to 394.00 ± 8.84 μg/gm creatinine in two weeks and was 156 ± 2 μg/gm creatinine at six months. These results indicate that the ISRD is a simple, practical and effective way of iodine supplementation in Xinjiang rural area of People's Republic of China. [Ed note: the abstract does not describe the nature or content of the ISRD.]