

APPENDIX E: TRANSLATION OF BACHINSKII PAPER

Bachinskii PP, Gutsalenko OA, Naryzhniuk ND, Sidora VD, Shliakhta AI.

Action of fluoride on the function of the pituitary-thyroid system of healthy persons and patients with thyroid disorders.. *Probl Endokrinol* (Mosk). 1985 Nov-Dec;31(6):25-9.

Abstract

Altogether 123 persons were examined: 47 healthy persons, 43 patients with thyroid hyperfunction and 33 with thyroid hypofunction. It was established that prolonged consumption of drinking water with a raised fluoride content (122 +/- 5 micromol/l with the normal value of 52 +/- 5 micromol/l) by healthy persons caused tension of function of the pituitary-thyroid system that was expressed in TSH elevated production, a decrease in the T3 concentration and more intense absorption of radioactive iodine by the thyroid as compared to healthy persons who consumed drinking water with the normal fluorine concentration. The results led to a conclusion that excess of fluorine in drinking water was a risk factor of more rapid development of thyroid pathology. Indicators of the fluorine content in daily urine provide most of the information on changes of the fluorine amount in the body.

(Note on units. In US fluoride concentrations are usually recorded as ppm or mg/L. For conversion, 1 micromol/L = 0.019 ppm, thus 122 micromol/L = 2.3 ppm)

Dept of Biochemistry (Director - Prof. P.P. Bachinskii) of the Poltava Medical and Stomatological Institute

It is known that in humans, animals and plants fluoride and iodine may exhibit antagonistic effects on several processes (7, 10, 14)

Inhabitants of the central part of Ukraine who utilize the water of Buchakcko-Kanevskiy water-bearing watershed may, in view of the high content of fluoride in the water (79 to 526 micromoles/liter), consume (fluoride) each day in amounts 2.6 to 50 micromoles per kilogram of body weight, versus a normal amount of 1 to 2.3 micromoles/kg. The concentration of fluoride in drinking water in accordance with GOST 2874-73 is no higher than 1.5 mg/l, that is, 79 micromoles/liter.(4, 7, 9, 13) (GOST is probably an acronym for a government agency and the whole term GOST 2874-73 probably refers to a regulation issued by that agency to establish permissible levels of toxic substances.)

The results of studies of the influence of fluoride on the functional status of the thyroid gland are conflicting. One report (8) states that the prolonged consumption of water with a high fluoride content exhibited a suppressive effect on the functional status of the thyroid gland in white rats, beginning with a fluoride concentration in the drinking water of 263 to 368 micromol/l, which corresponded to 13 to 18 micromol/kg of body weight.

The effect of fluoride in doses of 18 to 26 micromol/kg (368 to 526 micromol/l) was not a suppression but, on the contrary, an activation of the function of the thyroid system.

A number of authors (2, 6, 8) have shown that a fluoride content in the drinking water ranging from 102 to 421 micromol/l did not exert a significant influence on the activity of the thyroid in man. There was no measurable enlargement of the thyroid, nor pathological accumulation of radioactive iodine in the gland, nor increased frequency of disorders of this gland. A. S. Kasyanenko (7) proposes (as an explanation) the possible disruption of iodine metabolism and a suppression of the function of the thyroid gland in the presence of increased (79 to 526 micromol/l) intake of fluoride in the body. It is also reported that in persons consuming large amounts of fluorine, disorders of the thyroid gland are observed with significantly greater frequency (11, 12).

In view of the fact that there is a marked disruption in thyroid functions in areas of endemic "fluorosis" in humans, it is important to analyze fluoride concentrations not only in drinking water but in blood and urine samples, which is essential to a more accurate understanding of the kinetics of this chemical element in the human body.

The objective of our investigation was (to conduct) a comparative study of the functional status of the pituitary-thyroid system and to demonstrate a correlation between the concentration of fluoride in the drinking water and the body content of fluoride in healthy subjects and in those with hypo- and hyperfunction of the thyroid among permanent residents living in areas with differing concentrations of fluoride in the drinking water.

Materials & Methods

In a study of 123 individuals, 76 had pathology of the thyroid and hyperthyroidism; 43 of whom (in ages ranging from 18 to 58 years) had hyperthyroidism and 33 (in ages ranging from 20 to 55 years) had hypothyroidism; the control group consisted of 47 relatively healthy individuals (in ages ranging from 19 to 59 years). The subjects lived in two regions (districts), one of which had normal concentrations of fluorine in the drinking water, and the other with high concentrations of this element.

The intrathyroid phase of iodine metabolism (the I-131 uptake by the thyroid gland) was determined by the standard method. The hormonal activity of the pituitary (its content of thyrotropic (ie, thyroid stimulating) hormone – TSH) was determined with the aid of TSHK-PR ("Cea Sorin"). We studied the blood concentrations of thyroid hormones: thyroxin (T4), using the Byk-Mallinckrodt method (SPAC-T4), triiodothyronine (T3) with the use of the TRIK-PEG ("Cea Sorin")

Tests of fluorine concentration of in the drinking water, erythrocytes, serum and urine were done in accordance with the method of L.A. Golovanova (5) with the use of fluoride selective electrodes, EF U-1.

Results and Analysis (Discussion)

The results obtained (Table 1) indicate hyperfunction of the thyroid gland in 43 patients (increased concentrations of T3 and T4 in the serum in conjunction with increased radioactive iodine (I-131) uptake, and hypofunction in 33 patients (reduced concentrations of serum T3 and T4 along with reduced I-131 uptake).

In the control group and in subjects living in Region II there was a reduction in the concentration of T3 ($p < 0.05$) in conjunction with an increased I-131 uptake ($p < 0.05$) and increased concentrations of TSH in the serum ($p < 0.05$). This gave evidence of a stressed pituitary-thyroid system associated with abnormal iodine metabolism (a reduced production and intensified catabolic conversion of T3), since the concentrations of T4 in the serum of healthy persons of both regions were practically identical ($p < 0.5$).

In a similar way, the disruptive influence of fluoride on iodine metabolism was even more evident in the inhabitants of Region II. But since analogous disturbances of iodine metabolism are encountered in occasional individuals and in a region with a normal concentration of fluoride in the drinking water, it may be surmised that in such people there are other factors which contribute to abnormal thyroid function or even that it indicates an increased individual threshold level of fluoride in the drinking water.

The concentration of fluoride in the drinking water consumed by healthy people in Region I was in the range of 26 to 75 micromol/l, whereas the level of fluoride in the drinking water in Region II was significantly greater ($p < 0.05$) being in the range of 87 to 184 micromol/l.

The concentration of fluoride in the urine and serum of healthy individuals living in Region II was significantly greater ($p < 0.05$) in comparison with that in inhabitants of Region I. The concentrations of fluorine in the erythrocytes in clinically healthy persons living in Regions I and II were not statistically significantly different ($p < 0.1$).

Table 1: Test results of the pituitary-thyroid system of healthy (subjects) and patients with thyroid disorders living in regions with differing concentrations of fluorine in the drinking water.

Observed Group	Region	N subjects	I-131 Uptake 24 h %	Serum T4 levels umol/L	Serum T3 Levels umol/L	Serum TSH Levels umol/L
Hyperfunction group	I	21	61 + 7 p < 0.05	250 + 16 p < 0.05	5.2 + 0.7 p < 0.05	0.8 + 0.12 p < 0.05
	II	22	72 + 13 p ₁ < 0.05	261 + 23 p ₁ < 0.05	7.1 + 1.8 p ₁ < 0.05	0.6 + 0.08 p ₁ < 0.05
Hypofunction group	I	14	8.5 + 2.7 p < 0.05	26 + 7 p < 0.05	1.1 + 0.4 p < 0.05	51 + 11 p < 0.05
	II	19	9.8 + 1.3 p ₁ < 0.05	29 + 2 p ₁ < 0.05	1.0 + 0.1 p ₁ < 0.05	58 + 17 p ₁ < 0.05
Control group	I	17	24 + 3	97 + 8	2.8 + 0.3	2.4 + 0.2
	II	30	33 + 4 p < 0.05	94 + 6 p > 0.5	2.0 + 0.2 p < 0.05	4.3 + 0.6 p < 0.05

Footnote: p is the (statistical) probability of the difference in comparison with healthy subjects in Region I, while p₁ is the (statistical) probability of the difference in comparison with healthy subjects in Region II

Table 2: Fluoride concentration in drinking water of “practically” healthy (subjects) (ie, those who are clinically healthy for all relevant purposes) and in patients with thyroid disorders living in regions with differing fluoride levels

Observed Group	Region	N subjects	Fluoride in Water umol/L	Fluoride in urine umol/L	Fluoride in urine	Fluoride in Serum umol/L	Fluoride in Erythrocytes umol/24h.
hyperfunction group	I	21	63 + 8 p > 0.1	78 + 11 p > 0.5	112 + 23 p > 0.5	9.5 + 0.5 p > 0.05	24 + 1.5 p > 0.5
	II	22	114 + 11 p ₁ > 0.5 p ₂ < 0.05	152 + 27 p ₁ > 0.2 p ₂ < 0.05	203 + 49 p ₁ > 0.2 p ₂ < 0.05	10 + 0.5 p ₁ < 0.05 p ₂ > 0.2	27 + 5 p ₁ > 0.2 p ₂ > 0.2
Hypofunction group	I	14	58 + 5 p > 0.05	74 + 8 p > 0.5	82 + 11 p > 0.2	12 + 1 p > 0.5	29 + 5 p > 0.5
	II	19	134 + 24 p ₁ > 0.5 p ₂ < 0.05	146 + 22 p ₁ > 0.2 p ₂ < 0.05	194 + 38 p ₁ > 0.1 p ₂ < 0.05	15 + 1 p ₁ > 0.2 p ₂ > 0.05	32 + 0.8 p ₁ > 0.5 p ₂ > 0.5
Control group	I	17	52 + 5	78 + 9	98 + 15	11 + 0.5	29 + 5
	II	30	122 + 5 p < 0.05	124 + 9 p < 0.05	140 + 12 p < 0.05	13 + 0.5 p < 0.05	32 + 1.5 p > 0.1

Footnote: P₂ is the (statistical) probability of the difference in comparison with patients with thyroid disorders living in Region I

A study of the body's (obespechennosti) by fluorine in patients with hypo- and hyperactivity of the thyroid, depending upon the special characteristics of the region of habitation, enabled us to establish the following: the concentration of fluorine in the urine of patients with hyperactive thyroids who consumed drinking water with increased amounts of fluorine (87 to 184 micromol/l) was high ($p < 0.05$) compared with the level of the element in patients with (true) hyperthyroidism living in Region I. The excretion of fluorine in the urine in patients with hypofunctioning thyroids who consumed drinking water containing high levels of fluorine (87 to 300 micromol/l) was also high ($p < 0.05$) in comparison with the indices in inhabitants of Region I.

The determination of fluorine in 24-hour urine specimens enabled us to demonstrate a clear tendency toward increases in its content in the body due to dysfunction of the thyroid (Table 2). At the same time measurements of fluorine in the urine in micromol/l showed an evening up of differences in the fluorine content in the organism. The serum and erythrocyte concentrations of fluorine did not reflect differences in its content in drinking water, hence the most information is given by the findings on the content of fluorine in the 24-hour urine.

Similarly, the increased concentrations of fluorine in the drinking water of Region II, ranging from 87 to 300 micromol/l, materially changed the amount in the body as compared with Region I, but neither in the serum nor in the erythrocytes tested was there substantial change in the concentration of this element. It is known that fluorine is deposited chiefly in the bony tissues, and an excess amount of it is removed in the urine thanks to a protective mechanism, the role of which is played by the kidneys. (1, 3, 4).

Analysis of the results of the study of the content of fluorine in different constituent parts of the organism in healthy and sick subjects whom we tested, and a comparison of information provided by measures of the fluorine content of erythrocytes, serum and urine permitted us to conclude that the amount of the element present in the body is most adequately reflected by its level in the 24-hour urine. The data which we acquired on the higher concentration of fluorine in the erythrocytes than in the serum in all subjects tested suggests the existence of a membrane mechanism of active transport of fluorine against a concentration gradient, with the result that a higher concentration of fluorine is maintained in the erythrocytes than in the plasma. The observed membrane gradient of fluorine concentration is less than that in the case of potassium, but is essentially similar and, in all likelihood, biologically indispensable.

On the basis of the results of the studies (which we) conducted it is possible to conclude that the increased amount of fluorine in the drinking water (87 – 300 micromol/l) promotes the development of dysfunction of the thyroid gland in individuals.

The accumulation in the organism of excessive amounts of fluorine disrupts the metabolism of iodine and causes functional disturbances in the pituitary-thyroid system. With such disruption of this system, further stress may lead either to hyper- or to hypofunction of the thyroid, depending upon the coexistence of a number of factors,

which provides a basis for considering excessive amounts of fluorine in the body to be a risk factor for the pathology noted.

Conclusions

(1) The ingestion of drinking water with high concentrations of fluoride (122 +/- 5 micromoles per liter) leads, in healthy people, to stress of the functional status of the pituitary-thyroid system, as evidenced by a reduction in the concentration of T3, an increase in the production (by the hypothalamus) of TSH in the serum, and a more avid uptake of I131 by the thyroid tissue. This permits us to classify the excessive accumulation of fluorine in the body as a risk factor providing a basis for the development of thyroid dysfunction.

(2) Upon performing simultaneous determinations of fluorine content in the urine, red cells, serum and drinking water, the most informative indices concerning the kinetics of fluoride were those of its concentration in the urine.

(3) In healthy (persons) and in patients with thyroid disorders the concentration of fluorine in the erythrocytes was higher than in the serum, which attests to the presence of a mechanism of active transport of fluorine across the cell membrane.

References (this will need revision, translator was working from a fax copy with the letters rather blurred!)

(1) Avtsim (could be Avtsiy), A.P. -*The Pathology of Fluorosis*. Novosibirsk, 1981

(2) Verzhikoskaya, N.V. In the book: *Goiter disease*. Ed. A.K. Gorchakova. Kiev 1959

(3) Gaboviy, R.D. *Fluorine in stomatology and hygiene (sanitation)*. Kazan, 1969

(4) Gaboviy, R.D. *Hygiene (or sanitation) problems in fluoridation of the drinking water*. Moscow, 1979

(5) Golovanova, L.A. *The hygiene of work*. 1977, No.4, 55-57

(6) Zherduyenko, L.G. *The role of drinking (or nutrition in the broad sense) and fluoridation in the prevention of dental caries in children*. 1970 (Identified as his dissertation for a degree in medical sciences)

(7) Kasyanyenko, A.S. *Medical matters*. 1978, No. 10, 125-129.

(8) Knizhnikova, V.A. *Hygiene and sanitation*. 1959, No.1, 20-25

(9) Kavsan, N.I. In the book: *The hygiene of inhabited (populated) areas*. Kiev, 1974, 13,130-131

(10) Portyanko, L.A. In the book: *Microelements in the surrounding environment*. Ed. P.A. Vlasyuka. Kiev 1980, 39-42

(11) Sibora, V.D. et al. *Current problems in experimental and clinical endocrinology*. Kiev 1982

(12) Sibora, V.D. et al *Problems in endocrinology*. 1983, No.4, 32-35

(13) Stolyar, V.I. In the book: *Rational nutrition* Kiev, 1974, 10th edition, 85-90