THE ROLE OF FLUORINE AND IODINE IN THE DEVELOPMENT OF IODINE DEFICIT STATES. PREVENTION OF IODINE DEFICIT STATES

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S u m m a r y. The article covers the role of fluorine and iodine in the development of iodine deficit states in children that live in Poltava Province as well as the prevention of such states. Iodine deficiency prevention is considered to be the most effective and economical method and it is achieved by adding iodine-containing salts to the most consumable foodstuffs.
K e y w o r d s: nutrition, fluorine, iodine, children, prevention, mental retardation, cognitive abnormality.

The sufficient and balanced consumption of essential nutrients, or so called micronutrients (vitamins, microelement, minerals, essential fatty acids and essential amino acids) is an important component of both human and animal rational and healthy nutrition. The iodine deficit is one of the typical examples of micronutrient deficiency that manifests itself in a variety of disorders. "Iodine deficiency disorders" is a term used to define any disadvantageous effects (direct or relative) of the iodine deficit upon human growth and development, first of all upon child's brain maturing. The disorders are caused by hypothyroidism due to iodine deficit.

There are a large number of areas with iodine deficient biospheres. According to the assessment made by WHO and UNICEF, over 1.5 billion people live in such areas at the high risk of the development of the iodine deficiency disorders. 200 millions of them have been diagnosed goiter, 3 millions have endemic cretinism and remaining millions of people have slight psychomotor disturbances [2]. Though the iodine deficit has been eliminated in most developed countries, the different degrees of it still manifest themselves in some Western European countries. Since the consumption of iodine by the thyroid gland is excessive in endemic areas, the gland becomes more vulnerable to the radiation exposure which took place after the Chernobyl disaster [2]. It can be asserted that the evident cretinism cases in the iodine-deficient areas are only the tip of the iceberg while less apparent intellectual defects are difficult to be diagnosed and they are much more widespread. Bearing of mentally handicapped children is a fatal consequence of the iodine deficit. It has been proved [2] that if 10-15% of the population have enlarged thyroid glands, the intelligence quotients decrease accordingly.

One more school for children with learning difficulties has to be established annually in Ukraine (one third of which is an iodine-deficient area) though there are quite a number of such schools. The process can lead to the degradation of nation in some generations. The problem is so important that the International Council for the Control of Iodine Deficiency Disorders (caused by the direct or relative iodine deficit) has been established. The elimination of IDD is one of the UN priorities at the beginning of the third century. An appropriate program has been elaborated in Ukraine and approved by the Cabinet Order No. 1418 on 26th September 2002.

Together with employees of both the city and provincial sanitation and epidemiological centres we examined drinking water used by residents of Poltava City and Poltava Province for iodine, fluorine and radionuclide content.

Poltava Province is supplied water from three main water-bearing strata (Cenomanian - Lower Cretaceous, Buchak and Alluvial) except for Kremenchuk and Komsomolsk towns that are supplied water from the Kremenchuk Reservoir and the Dniprodzerzhynsk Reservoir. It should be noted that 42.3% of the province area supplied the water from the Buchak water-bearing stratum characterized by high fluoride concentrations, up to 2.1-2.6 mg/l, which is 2-2.5 times as much as the optimal value (Table 1). The occurrence analysis of thyroid pathologies in Ukraine and Poltava Province in particular indicates that the number of thyroid disorders increased and their structure changed during the period from 1980 to 2003 (the comparison with all-Ukrainian data was made with the help of the *Key Performance Indicators of the Ukrainian Endocrinological Service* annual published by the Ministry of Public Health of Ukraine and Komissarenko Institute of Endocrinology and Metabolism, Academy of Medical Sciences of Ukraine, over the past 25 years).

Table 1. The description of water-bearing strata.

Water-bearing strata	Area covered, %	Population, ths people	Depth, m	Concentration in Drinking Water						
				I_2, mg/l	F_2, mg/l	K= I_2/ F_2	Ra_{224}, 10^{-2} Bq/l	Ra_{226}, 10^{-2} Bq/l	U_{236}, 10^{-2} Bq/l	Σ, 10^{-2} Bq/l
Cenomanian - Lower Cretaceous	15.4	336.5±84.1	1,012.1± 127.7	0.09±0.01	0.9± 0.06	0.1± 0.01	1.6± 0.6	1.9± 0.4	0.2± 0.1	3.6± 0.8
Buchak	42.3	134.5±3.58	144.9± 9.2	0.08± 0.01	1.02± 0.14	0.08± 0.02	1.6± 0.3	1.5± 0.3	0.5± 0.2	3.6± 0.6
Alluvial	3.8	1.3± 0.09	32.5± 2.5	0.08± 0.01	0.8± 0.01	0.1± 0.01	1.8± 0.01	1.0± 0.01	0.3± 0.001	3.1± 0.6

Such diseases as 1st and 2nd degree nodular goiter, thyroiditis, thyroid carcinoma, simple and unspecified goiter started to occur in reports in 1989 (earlier 3rd to 5th degrees were only recorded). In the past 13 years the occurrence of thyroiditis in Poltava Province has become 40.7 times as much (in Ukraine 22.1 times as much), simple goiter – 9.3 times as much (in Ukraine 4.8 times as much), nodular goiter – 7.9 times as much (in Ukraine 7.1 times as much), thyroid carcinoma – 2.0 times as much (in Ukraine 2.5 times as much), hypothyroidism – 3.2 times as much (in Ukraine the figures are the same) and toxic diffuse goiter – 1.1 times as much (in Ukraine 0.9 times as much). The trends of thyroid disorders between 1980 and 2003 in Poltava Province and in Ukraine are displayed in the Table 2.

Table 2. The occurrence of thyroid disorders (per 100 ths people) in Poltava Province and in Ukraine.

Diseases	Area	1980	1989	2003	Increase in the past 13 years
Simple and unspecified goiter	Poltava Province	30.2	102.9	955.1	9.3
	Ukraine	66.9	589.0	2,844.5	4.8
Nodular goiter	Poltava Province		30.5	240.6	7.9
	Ukraine		38.6	274.6	7.1
Thyroiditis	Poltava Province		4.3	174.9	40.7
	Ukraine		10.3	227.8	22.1
Toxic diffuse goiter	Poltava Province	61.1	79.0	90.7	1.1
	Ukraine	62.7	87.2	80.8	0.9
Hypothyroidism	Poltava Province	30.3	36.2	117,9	3,2
	Ukraine	32.4	40.6	132.3	3,2
Thyroid carcinoma	Poltava Province		9.0	4.5	2.0
	Ukraine		11.0	4.3	2.5

In our opinion, the gradual reduction of iodine concentrations in the environment in Poltava Province (Table 3) is the trigger for thyroid pathologies, and the iodine-fluorine derangement conditions the structure of thyroid pathologies in the area. As we can see, the areas with the increased number of 1st degree diffuse goiter and hypothyroidism cases are characterized by a low iodine-fluorine coefficient and otherwise a high iodine-fluorine coefficient is typical for the areas with the increased number of thyroid carcinoma, thyroiditis and toxic diffuse goiter cases (Table 3). We think that the structure of thyroid pathologies is also influenced by total radionuclide concentrations in the environment. A higher total radionuclide concentration is characteristic for the areas with the increased number of thyroid carcinoma cases and contrariwise a lower total radionuclide concentration is observed if the increased number of nodular goiter, thyroiditis and hypothyroidism cases take place (Table 3).

Table 3. Thyroid clinical entity occurrence, iodine-fluorine coefficients and total radionuclide concentrations in two area groups in Poltava Province.

Clinical entity	Area group	Occurrence, per 10 ths people	Iodine concentra-tions, mg/l	Fluorine concentra-tions, mg/l	Iodine-fluorine coefficient	∑ radionuclide concentration, 10^{-2} Bq/l
1st degree diffuse goiter	I	34.99±3.65	0.08±0.002	1.06±0.15	0.12±0.03	2.33±0.19
	II	115.4±9.6*	0.06±0.001	0.91±0.11	0.11±0.03	2.19±0.13
2nd and 3rd degree diffuse goiter	I	8.59±1.45	0.07±0.005	1.05±0.11	0.11±0.03	2.36±0.14
	II	38.47±4.71*	0.07±0.01	0.8±0.03*	0.11±0.02	2.11±0.16
Nodular goiter	I	11.99±1.2	0.08±0.01	0.99±0.09	0.11±0.03	2.42±0.15
	II	40.16±5.8*	0.08±0.01	0.97±0.07	0.11±0.02	1.94±0.11*
Thyroiditis	I	9.73±0.78	0.07±0.004	1.07±0.1	0.11±0.01	2.41±0.13
	II	33.32±4.58*	0.09±0.002*	0.65±0.06*	0.14±0.01*	1.76±0.16*
Toxic diffuse goiter	I	6.05±0.36	0.08±0.004	0.97±0.05	0.12±0.02	2.23±0.14
	II	14.4±0.82*	0.07±0.005	1.01±0.04	0.13±0.03	2.4±0.14
Hypo-thyroidism	I	8.70±0.76	0.07±0.005	1.06±0.02	0.11±0.03	2.49±0.16
	II	18.44±0.86*	0.07±0.001	0.83±0.01*	0.11±0.02	1.9±0.15*
Thyroid carcinoma	I	0.22±0.03	0.07±0.006	1.05±0.01	0.12±0.03	2.14±0.14
	II	0.77±0.02*	0.06±0.006	0.83±0.01*	0.13±0.05	2.71±0.12*

*Note: * - the difference is reliable acc 2nd group available figures*

Tymchenko and co-authors [3] consider Ivano-Frankivsk Province to be a strongly iodine-deficient area and Zhytomyr Province to be a moderately iodine-deficient area. Besides, some authors [2] state that radioactive fallout occurred in 4 districts of Zhytomyr Province.

Poltava Province is also referred to moderately iodine-deficient areas [3]. We studied the 1989 to 2003 trends of goiter endemia in the areas and we have displayed the findings in the Table 4. Simple and unspecified goiter prevailed in all the areas both in 1989 and 2003. The next position was occupied by nodular goiter, with Dnipropetrovsk Province at the top of the list, then Zhytomyr Province, and Ivano-Frankivsk Province at the bottom. Thyroiditis follows them, with Kyiv Province at the top, then Zhytomyr Province followed by Ivano-Frankivsk Province. The trends of hypothyroidism, thyroid carcinoma and toxic diffuse goiter are inverse, for example, the number of TDG cases decreased by 2003 (Table 4).

Table 4. Thyroid disorders (%) in Ivano-Frankivsk, Zhytomyr and Poltava provinces and in Ukraine in whole in the mentioned periods.

Disease	Area	1989	2003
Simple and unspecified goiter	Zhytomyr Province	83.6	83.2
	Ivano-Frankivsk Province	70.0	91.0
	Poltava Province	39.3	60.3
	Ukraine	75.8	79.7
Nodular goiter	Zhytomyr Province	5.8	9.2
	Ivano-Frankivsk Province	7.9	3.6
	Poltava Province	11.6	15.2
	Ukraine	5.0	7.7
Thyroiditis	Zhytomyr Province	1.4	2.9
	Ivano-Frankivsk Province	1.0	1.2
	Poltava Province	1.6	11.0
	Ukraine	1.3	6.4
Toxic diffuse goiter	Zhytomyr Province	5.2	2.0
	Ivano-Frankivsk Province	12.6	2.0
	Poltava Province	30.2	5.7
	Ukraine	11.2	2.4
Hypothyroidism	Zhytomyr Province	3.4	2.5
	Ivano-Frankivsk Province	8.2	2.2
	Poltava Province	13.8	7.4
	Ukraine	5.2	3.7
Thyroid carcinoma	Zhytomyr Province	0.6	0.09
	Ivano-Frankivsk Province	0.3	0.03
	Poltava Province	3.4	0.3
	Ukraine	1.4	0.1

The Provincial Psychological Medical Pedagogical Commission, which makes records of children with the congenital and acquired diseases of intellectual or mnemonic nature (such as autism, mental retardation, hearing disorders, visual impairments etc.), reports that personalized learning groups are formed at specialized kindergartens and schools. We have found out that the number of children with such pathologies increased dramatically in the past 12 years. Thus, in 1992 there were 588 such children, but in 2003 there were 2137 of them, so their number went up 3.6 times (Table 5, Fig. 1).

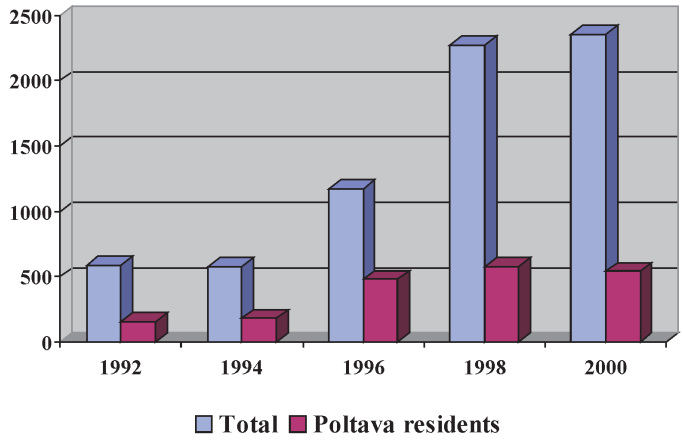

Fig. 1. Number of children that need to be taught at specialized schools.

Yarmonenko (1988) states that endocrine glands are radioresistant, which can be said about the thyroid gland as well. Its radiosensitivity increases rapidly while in the state of hyperplasia. Hyperplasia (or 1st-2nd degree goiter) is dominant over other thyroid pathologies during the post-Chernobyl period.

It can be assumed that the short-lived radionuclides (Ra224, J131) bombard tissues and deprive them of radioprotection and then the exposed tissues are influenced by the long-lived radionuclides (U234, U235, U238, Ra226, Sr89, Sr90 etc.)., i.e. short-lived radionuclides impact the genesis of thyroid hyperplasia and the long-lived radionuclides impact the genesis of thyroid carcinoma. Therefore, patients with thyroid hyperplasia should be considered as a thyroid carcinoma high-risk group, and of course, the group should be the first to be applied preventive measures to.

Table 5. Number of children that need to be taught at specialized schools and kindergartens recorded by the Provincial Psychological Medical Pedagogical Centre for residents of Poltava City and Poltava Province

Record year	Total	Residents of Poltava City
1992	588	156
1993	605	159
1994	580	181
1995	1168	503
1996	1173	480
1997	1778	575
1998	2274	578
1999	2261	574
2000	2354	542
2001	2371	624
2002	2389	624
2003	2137	523

While evaluating the environmental situation in Poltava Province, one can note that this is a moderately iodine-deficient area due to low iodine concentrations in all water-bearing strata Poltava Province is supplied the water from. Iodine deficiency is aggravated by high fluoride concentrations in Buchak water-bearing stratum that supplies water to 42.3% of the province area. When reaching the thyroid tissues fluoride as a more active halogen blocks thyroid peroxidase and iodide organification in the thyroid gland, which leads to the inhibition of thyroid hormone synthesis. Fluoride is also a powerful free radical lipid peroxidation-inducing agent. The accumulation of free radical lipid peroxidation by-products and end products in the thyroid tissues causes free radical damage, which in total decreases the number of functional cells in the thyroid tissues. Hyperplasia and hypertrophy develop under the influence of TSH as in a feedback loop. Usually, when reaching thyrocytes, iodine generates iodothyronines and iodolactones, lipid compounds that inhibit local tissue growth factors such as insulin-like growth factor, epidermal growth factor, main fibroblast growth factor and others. When the blockade is absent (fluoride causes the inhibition of iodine capture) the growth factors trigger proliferation processes. The number of somatic mutations increases and nodules, cysts, adenomas etc appear in the hyperplastic gland. The blockade of thyroid peroxidase and thyrocyte loss as a result of free radical damage, immune destruction and radiation effect cause the inhibition of thyroid hormone synthesis; then subclinical hypothyroidism and later overt hypothyroidism develop and have negative impact on human physical and intellectual development. The proposition can be proved by the high percentage of autoimmune thyroiditis in Zhytomyr Province (55.2%) and Poltava Province (54.8%) while idiopathic hypothyroidism cases are absent in the areas; in Ivano-Frankivsk Province, the idiopathic hypothyroidism rate was 41.5% in 1978, and the autoimmune thyroiditis rate was only 5.3% (according to the Performance Indicators of the Ukrainian Endocrinological Service 1978).

IDD prevention is much more effective than the elimination of iodine deficiency consequences; some of them (mental retardation and cretinism) are virtually irreversible. Table 6 shows minimum daily requirements for iodine. As we can see they are not high; a man consumes 3-5g of iodine over his life. The minimum intake of iodine should be provided daily, year by year. Once you forget it, iodine deficiency reminds you about it immediately.

Table 6. Minimum daily requirements for iodine (WHO recommended, 2000).

Age group	Requirement for iodine, microgram/day
Babies (under 1)	90
Infants (under 6)	90
Schoolchildren (under 12)	120
Teenagers over 12 and adults	150
Pregnant and nursing women	200
Elderly people	100

Some authors [1, 3] state that actual intake of iodine in Ukraine is only 40-60 micrograms/day, which is a third of the recommended level. The insufficient intake of iodine threatens the population dramatically, so mass and group preventive measures should be taken with due consideration for local iodine deficiency peculiarities. There are individual, group and mass iodine deficiency preventive methods.

Prevention of individual iodine deficiency consists in the consumption of iodine rich foods (sea fish, seafood) and medications that provide physiological iodine intake: Iodide-Pharmac-100, -200 (Pharmac, Ukraine), Iodomarin-100, -200 (Berlin-Chemie, Germany) and Iodide-100, -200 (Nycomed, Norway) (Table 7). The prevention method requires an individual to be appropriately trained and motivated.

Group prevention of iodine deficiency stipulates for the prescription of iodine-containing medications (Iodide-Pharmac-100, -200 (Pharmac, Ukraine), Iodomarin-100, -200 (Berlin-Chemie, Germany) and Iodide-100, -200 (Nycomed, Norway)) for the IDD high-risk groups (infants, teenagers, pregnant and nursing women etc) under medical control and the regular long-term consumption of a fixed physiological iodine dose: for children under 12 – 50 to 100 micrograms/day; for teenagers and adults – 100-200 micrograms/day; for pregnant and nursing women – 200 micrograms/day.

Table 7. Iodine concentrations in some foods (per 100 g of product).

Foods	Iodine concentration, microgram	Foods	Iodine concentration, microgram
Fish: Haddock	416.0	Rice	2.2
Salmon	260.0	Hen's egg	9.7
Shrimps	190.0	Vegetables: Spinach	20.0
Plaice	120.0	Garden radish	8.0
Cod	120.0	Potatoes	3.8
Grouper	74.0	Cucumbers	2.5
Halibut	52.0	Fruit: Apples	1.6
Fresh herring	66.0	Pears	1.0
Herring in a sauce	6.0	Cherries	0.3
Tuna	50.0	Milk: Breast milk (from 10th day after childbirth)	6.3
Eel	4.0	Cow's milk (1.5% fat content)	3.7
Trout	3.5	Dairy products: Butter	4.4
Baked goods	3.0-8.5	Condensed milk	9.9
Cereals	1.5-4.5	Cheese (40% fat content)	3.4
Flour	2.0-3.0	Kefir (3.5% fat content)	3.7
Rye bread	8.5	Meat (medium fat content): Pork	3.0
White bread	5.8	Beef	3.0
Oat flakes	4.0	Veal	2.8

Mass prevention of iodine deficiency is considered to be the most effective and more economical method; it is achieved by adding iodine-containing salts (iodide or potassium iodate) to the most consumable foodstuffs (table salt, bread, water and butter). The annual cost of iodine deficiency prevention by salt iodination does not exceed $0.1 per capita and it is covered by consumers themselves.

CONCLUSION

Iodine deficiency prevention is considered to be the most effective and economical method and it is achieved by adding iodine-containing salts to the most consumable foodstuffs.

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