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#### **Review Article**

# lodine Prophylaxis - Global Action

#### Szybiński Zbigniew\*

Department of Endocrinology, Jagiellonian University, Poland

#### Abstract

**Background:** lodine deficiency is a worldwide public health problem affecting around 4 billion people. It manifests clinical consequences: goiter, hypothyroidism, cretinism and negative economic consequences. In 1986 lodine Global Network was established.

**Objectives:** The aim of this article is presentation of the model of iodine prophylaxis as a global prophylactic program to prevent iodine deficiency on the population level. Iodine plays a leading role in metabolic pathways as integral part of the thyroid hormones - thyronine and thyroxin and as a strongest antioxidant.

**Methods:** According to WHO recommendation actual model of iodine prophylaxis is based on iodization of salt (NaCl) and on additional dose 100-150µg of iodine for pregnant and breast feeding women. The monitoring of the effectiveness of the model is based on mass screening of neonatal TSH and determination of urinary iodine concentration.

**Results:** In majority of European countries iodine supplementation has been recognized as adequate and it allowed to eliminate on the population level goiter and cretinism and to assure proper iodine supplementation for pregnant and breast feeding women,

**Conclusion:** ICCIDD lodine Global Network is powerful alliance to assist countries in elimination of iodine deficiency on the population level. In 2014 the organization was named lodine Global Network (IGN).

#### **INTRODUCTION**

Iodine was discovered in 1811 by French manufacturer Bernard Courtois in seaweed and up to the present time iodine is extracted from seaweed for manufacture. The natural resources of iodine are: seawater, seaweeds, and saltpeter-nitrate deposit in Chile. In 2014 new natural of iodine as iodides with concentration of 130mg/dm-3 has been discovered in Poland.

Iodine deficiency is a worldwide public health problem affecting around 4 billion people It manifests as- especially in schoolchildren in the mountains- goiter, a clinical consequences - hypothyroidism leading to neurological diseases (cretinism), disturbances of the development and negative economic consequences as well [1-3].

#### **CHEMICAL PROPERTIES OF IODINE**

Iodine belongs to the VII group of the Mendeleyev's periodic tables with atomic mass 126.9 and boil temperature 84.25°C, at room temperature sublimes, and evaporate during of cooking.

Iodine is very strong antioxidant (Table 1) and in the cells creates negative electric potential – 0,54 V.

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#### \*Corresponding author

Szybiński Zbigniew, Department of Endocrinology, Jagiellonian University, Collegium Medicum, Krakow, Poland, Email: szybin@cm-uj.krakow.pl

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Due to this property, iodine very easy creates chemical compounds and in this way iodine became an essential component of the crucial thyroid hormones: thyrosine and thyroxine that regulate all metabolic pathways.

Iodine at high concentration in alcoholic solution - known as "tincture of iodine" is administered as a strong antiseptic. At this concentration is poisonous and may cause damage to skin and other tissues.

#### Role of iodine in the metabolic pathways

Iodine is absorbed as iodides from the bloodstream by upper intestine and is taken up by thyroid gland, gastric mucosa, salivary glands and mammary glands in pregnancy and breast feeding. Due to high negative potential produced by the iodine a special mechanism transporting iodine across the cellular membrane starts.

At baso-lateral part of thyrocytes a specific enzyme - Natrum-

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Table 1: Chemical property of iodine as antioxidant.
_2 J = J + 2e = - 0,54 V
_2
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Iodine - Symporter (NIS) is allocated. It is protein, contains 643 amino acids and its part with amino- domain is directed out of the cell membrane and carboxyl-domain to inside of cell. It allows to transport 2 atoms of natrium and 1 atom of iodine against electrochemical gradient generated by Na+/K+ ATPase. In the thyroid gland iodine ions, are transported from the baso-lateral to the apical membrane of the thyrocytes due to other transporters: Pendrin the product of Pendred Syndron gene (PDS), and Apical Iodine Transporter (AIT) both located in the apical membrane of thyrocytes [4,5].

Thyroid hormones biosynthesis is carry out at the apical pole of thyrocytes and is catalyzed by thyroperoxidase (TPO) in the presence of  $H_2O_2$  (Table 2).

Generator of H<sub>2</sub>O<sub>2</sub> it is glycoflavoprotein called Duox, located in the apical membrane of thyreocyte. Tyrosyl residues in thyroglobulin (Tg) allocated in the follicular lumen are iodised to T3 and T4, and small amounts of T4 may be converted by 5-deiodinase to T3. First step of thyroid hormone secretion is hydrolysis of Tg, and following that, T3 and T4 are released into the bloodstream. Secretion of T3 and T4 is regulated by Thyroid Stimulating Hormone (TSH) produced by the pituitary under the control of hypothalamic Thyrotropin Releasing Hormone (TSH-RH) on the basis of feedback mechanism. TSH controls all stages of thyroid hormones synthesis and iodine uptake by thyroid gland as well. Thyroid hormone synthesis is controlled by iodine on the basis of feedback mechanism, and by other factors: Tumor Necrosis Factor - alfa (TNF-alfa) and Insulin-Like Factor Ngamma (IFN-gamma) - both inhibit TSH action. The day-night biorhythm influences strongly the TSH action: TSH - RH secretion is inhibited during day and activated at night, creating typical for TSH secretion biorhythm [5,6]. TSH is a very sensitive marker of iodine deficiency in neonates.

In 2001 WHO UNICEF and ICCIDD recommended determination of TSH in neonatal blood as a criterion of the degree of iodine deficiency and neonatal mass screening started [7].

On the tissues level an acting thyroid hormone is triiodothyronine controlling all metabolic pathways of the all tissues starting from the second year of life when the T-3 receptors are ready to act. T-3 interacts with nucleus receptors of the tissues. Two types of T-3 receptors have been recognized: human thyroid receptor-alfa 1 (HTR-alfa1) and human thyroid receptor-beta 1 (HTR-beta 1). It reflects different sensitivity of the tissue. For instance in brain there are mainly HTR-alfa1, in liver – HTR-beta 1 and in cardiac muscle - both types of these receptors. The most important target is cardiac muscle where T3 action results in increasing the inotropic action. In the digestive tract in small intestine T3 increases absorption of carbohydrates and the number of receptors for Low Density Lipoproteins (LDL).

In the muscles T-3 develops a catabolic action and on the level of fatty tissue increases its lipolitic properties. In all tissues -apart from brain, uterus, testis and hypophysis -T3 increases oxidative processes [5,6].

# Role of iodine in the pregnancy and in the postnatal period

In pregnancy iodine demand is markedly increased. Iodine

Table 2: Thyroid hormones biosynthesis.
J + peroxidase + $H_2O_2$ + tyrosyl = monoiodotyrosine + HO + e
2J + peroxidase + $H_2O_2$ + tyrosyl = diiodotyrosine + $H_2O$ + e
$2e + H_2O_2 + 2H = 2H_2O$
Monoiodothyrosine + diiodothyrosine = triiodothyrosine (T3)
2 diiodothyrosine = fouriodothyrosine (T4).

plays a crucial role in development of the central nervous system of neonate [7]. It is due to increased activity of the mother's thyroid gland and increased production of thyroxine when in the first trimester of pregnancy the thyroid of the fetus cannot produce this hormone. Additionally, during pregnancy iodine as a strongest antioxidant is transported to the tissues of fetus [8].

In 2007 WHO formulated recommendation on iodine requirement dose for different groups of age and pregnant and breast feeding women (Table 3).

Daily requirement of iodine in European diet may be covered by diet alone only in about 60% and the rest should be supplied by iodine prophylaxis based on the iodization of salt. In the sea-side areas only every day diet may cover recommended requirement of iodine. However, independently pregnant and breast feeding women should receive additional daily dose of iodine 100-150 $\mu$ g of iodine presenting a very rational balanced every day diet. Iodine prophylaxis systems are necessary to get recommended amount of iodine [8].

#### THE CONSEQUENCES OF IODINE DEFICIENCY

Iodine deficiency leads to serious consequences on the population level. Over 1/3 global population is exposed to iodine deficiency and over 600 millions have enlarged thyroid gland [1-3]. Insufficient iodine supply leads to impairment of thyroid hormone synthesis and is manifested as diseases termed iodine deficiency disorders (IDD). These are endemic goiter, impaired thyroid function, irreversible brain damage - cretinism due to inhibition of development of the thyroid gland in pregnancy [9,10].

The first observation in Poland on enlarged thyroid gland was performed in XIX century by Polish philosopher and scientist geologist Stanisław Staszic (1755 -1826) [11], however at that time a role of iodine was not known. The most serious effect of iodine deficiency in Poland –cretinism-was for the first time described by Ciechanowski in 1898 [12].

In iodine deficiency disorders gastric and mammalian glands cancers are also observed.

Iodides are transported into the gastric cells on the metabolic

Table 3: Daily Iodine Requirement Dose (WHO 2007).			
Catagery	Daily iodine requirement [µg/day]		
Nursery-Children 0 - 55 months	90		
Schoolchildren 6 - 12 years	120		
Adults > 12 years	150		
Pregnant and breast feeding women	250		

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passway with sodium iodide symporter (NIS) in gastric mucosa. Iodine plays important role as antioxidant protecting against gastric cancer and some inflammation processes [13]. Gastric cancer morbidity rate in Poland in the period of time 1999-2004 diminished by 23% for men and 27% for women. It would be linked with reduction of salt consumption due to a role of sodium as risk factor of neoplastic processes [14]. It should be also linked with effective model of iodine prophylaxis in Poland [23].

A very serious consequence of iodine deficiency may appear due to nuclear power plant emergency. The radioactive isotopes are released from operating reactors: 131-I, Sr-50 strontium, 239-Pt- platinum and others in smaller concentration. Especially radioactive isotope 131-I emitting gamma and beta radiation is danger due to its accumulation in the thyroid gland and it is a risk factor for thyroid cancer and thyroid hypofunction.

Nuclear power plants are currently operating in 34 countries and United States of America, France, Russia, South Korea and China generate more than 2/3 of the total nuclear energy over the world. In the United States of America 19.5% of electricity is generated from nuclear reactors. In 2017 American Thyroid Association published a special statement on the distribution KI on the population level in the event of nuclear accident [15]. A similar action was undertaken in Poland after Chernobyl accident [16].

#### **IODINE PROPHYLAXIS**

The World Health Organization indicated in 1994 main strategy for iodine prophylaxis- Universal Salt Iodization. In Poland an actual situation on Iodine Deficiency Disorders has been recognised [17-20] and new model of iodine prophylaxis was introduced in 1996 [21,22]. It contains: obligatory iodization of household salt and neonates formula, and recommendation on addition daily dose of iodine for pregnant and breast feeding women. This model allowed to eliminate endemic goiter in school children, cretinism in mountainous areas, and markedly diminished thyroid and gastric cancer. WHO in 2002 classified Poland as a country with optimal iodine daily intake on the population level [23,24]. However, according to the WHO recommendation formulated in Paris [25] and Luxemburg [26] daily salt intake should be limited when sodium is the main risk factor of hypertension and arteriosclerosis.

person/day].		
European countries	Daily intake of natrium chloride [g/ person/day]	
Belgium	8.3 - 8.7	
UK	9.7 - 11.7	
Italy	9.2 - 10.8	
Germany	8.2 - 8.8	
Portugal	l 9.0 -11.0	
Denmark	8.2 - 8.4	
France	7.9 - 8.4	
Poland	1998 - 15.0, 2003 - 13.5, 2009 - 11.5	
WHO recommendation 5.0g NaCl / person / day		

**Table 4:** Daily intake of natrium chloride in the European countries [g/

In 1998, consumption of both types of salt in Poland was 15.0g/day/person, in 2003 - 13.5 and in 2011 - 11.5 respectively [14,27]. In Poland household salt only is iodized with 20-40mg/ KI/kg but it represents over 40% of the consumed salt which explains the good results of iodine prophylaxis on the population level. It must be stressed that diminishing consumption of salt, decreases also daily iodine intake and needs new approach to the model of iodine prophylaxis implemented in Poland. The additional standardized carriers of iodine should be introduced in the food market to protect proper iodine consumption, as recommended by WHO. The important additional carrier of iodine supplementation may be table and mineral waters containing a standardized concentration of iodine [0.10-0.20mg/L], which should be a regular part of a balanced diet. In cooperation with National Research Institute of Animal Production in Balice [Prof. F. Brzóska] new model of iodization of the cows licks was introduced and iodine concentration in milk increased from 20-40 to 140-160µg of iodine/L [28]. It may play important role as additional carrier of iodine for school children and pregnant and breast feeding women.

#### **IODINE GLOBAL NETWORK**

In 1986 the Iodine Global Network- non-government organization was established [29]. In this same year International Council for Control of Iodine Deficiency Disorders (ICCIDD) was launched in Kathmandu - Nepal. ICCIDD cooperated together with UNICEF, the Micronutrient Initiative and Global Aliance for Improved Nutrition to eliminate iodine deficiency. In 2012 ICCIDD Global Network was formed from the ICCIDD, and Network for Sustained Elimination of Iodine Deficiency launched in 2002.

Finally in 2014 this powerful alliance was renamed again the Iodine Global Network (IGN) [30]. It plays leading role as scientific advisor on iodine nutrition. This network cooperates with over 100 regional and national coordinators and with the Global Alliance for Improved Nation the Micronutrient Initiative and UNICEF who represent global efforts to eliminate Iodine Deficiency Disorders.

It must be stressed that during last 30 years a big progress took place especially in the European countries (Table 5).

Among 37 European countries seven only (10.3%) represent mild adequate in iodine supplementation with urinary iodine concentration (UIC) 75-91 $\mu$ g/L. Around 90% of the European countries represents adequate iodine supplementation with UIC 106 - 251 $\mu$ g/L.

However these results must be monitored constantly by means of TSH mass screening and local programs for elimination of iodine deficiency. Additional global problem it is overconsumption of salt (NaCl) - risk factor of hypertension and some neoplastic processes -the main carrier of iodine in iodine prophylaxis models. It must be compensated by other iodine carriers mainly cow milk and mineral water with proper iodine concentration. It is particularly important for pregnant and breast feeding women who should receive additional 100-150 $\mu$ g of iodine under control of the physician.

The main goals of the Iodine Global Network are as follows [30].

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Table 5: Iodine Prophylaxis in European Countries.			
Number of the Effectiveness (Urinary)	Concentration	(Range - µg/L)	
30	Adequate	106 - 251	
7	Mild adequate	75 - 91	

- Supporting and harmonization of national and international programs for elimination of iodine deficiency.
- To advocate for political will and increased attention and resources for iodine programs.
- To identity and help address challenges to iodine programs.
- To support and strengthen national programs and fortification coalitions through consistent programmatic guidance.
- To identify and address scientific questions and influence research agenda in order to increase the effectiveness of iodine programs.

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