Review article

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PREVENTION OF NUCLEAR DAMAGE CAUSED BY IODINE AND CESIUM RADIONUCLIDES TO THE THYROID, PANCREAS AND OTHER ORGANS

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In times of danger of severe international conflicts with fear of the use of atomic weapons and accidents in nuclear power plants, a so-called "Disaster Medicine" has been created to reduce the damage in affected populations and territories. Radionuclide contamination in terrestrial ecosystems has nowadays reached a dangerous level. The most frequent and studied artificial radionuclides are iodine (131-I) and cesium (137-Cs and 134-Cs), which are both on the rise in the world. In humans, these elements are captured and metabolized by the thyroid, pancreas, mammary and salivary glands, cerebrospinal fluid and brain, thymus and numerous other organs and excrete with stool and urine. In organs, these radionuclides are a serious danger that can cause cancers, and through inflammatory, carcinogenic and necrotic mechanisms also thyroiditis, pancreatitis and functional deficiencies as well as diabetes mellitus, hypothyroidism and mental damage. The Author reports autoradiographic and scintigraphic studies describing some, little-known, damage to organs caused by radionuclides and in particular, pancreatic and thyroid cancer, chronic pancreatitis, thyroiditis and diabetes mellitus, whose incidence rate is gradually rising worldwide. Some methods of radionuclide removal and cancer prevention are also suggested.

Keywords: radio-iodine, radio-cesium, thyroid cancer, pancreatic cancer, pancreatitis, diabetes mellitus.

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Обзорная статья

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ПРОФИЛАКТИКА РАДИАЦИОННОГО ПОРАЖЕНИЯ ЩИТОВИДНОЙ ЖЕЛЕЗЫ, ПОДЖЕЛУДОЧНОЙ ЖЕЛЕЗЫ И ДРУГИХ ОРГАНОВ РАДИОНУКЛИДАМИ ЙОДА И ЦЕЗИЯ

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Во времена опасности серьезных международных конфликтов с угрозой применения атомного оружия и аварий на атомных электростанциях была создана так называемая «медицина катастроф» для уменьшения ущерба пострадавшему населению и территориям. Радионуклидное загрязнение наземных экосистем в настоящее время достигло опасного уровня. Наиболее распространенными и изученными искусственными радионуклидами являются йод (131-I) и цезий (137-Cs и 134-Cs), которые образуются в мире все в большем количестве. У человека эти элементы захватываются и метаболизируются щитовидной железой, поджелудочной железой, молочными и слюнными железами, обнаруживаются в спинномозговой жидкости, головном мозге, тимусе и многих других органах и выделяются с калом и мочой. В органах эти радионуклиды представляют серьезную опасность, поскольку могут вызывать рак, а также, путем активации воспалительных, канцерогенных и некротических механизмов, тиреоидит, панкреатит и нарушение функций поджелудочной железы, сахарный диабет, гипотиреоз и психические расстройства. Автор статьи приводит данные об авторадиографических и сцинтиграфических исследованиях, описывающих некоторые малоизвестные поражения органов, вызванные радионуклидами, в частности, рак поджелудочной и щитовидной железы, хронический панкреатит, тиреоидит и сахарный диабет, заболеваемость которыми неуклонно растет во всем мире. В работе также предложены некоторые методы удаления радионуклидов и профилактики рака.

Ключевые слова: радиоактивный йод, радиоактивный цезий, рак щитовидной железы, рак поджелудочной железы, панкреатит, сахарный диабет.

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Introduction. In times of danger of serious international conflicts with concerns about the use of atomic weapons or accidents in nuclear power plants, a so-called "*Disaster Medicine*" has been created. Its task is to deal with and reduce the resulting damage to the affected populations and territories. There are two types of damage: severe, most clearly evident, and chronic damage of more difficult and controversial interpretation and treatment. Acute damage are studied and treated by "*Emergency Medicine*", while chronic damage requires long periods of observation, with complicated and often controversial statistical studies. The Author tries briefly to describe some, little studied, chronic damage in organs capable of capturing some of the most important and frequent radionuclides such as Iodine and Cesium, and thyroid (TC) and pancreatic cancers (PC) nowadays progressively increasing worldwide.

Controversy on low radiation dose damage. There is considerable controversy about the accuracy of the methods used to identify the biological damage caused by nuclear radiation. Since 1986, the total toll of the nuclear disaster has not been agreed; as the medical journal "*The Lancet*" (2017) and other sources have noted, it remains contested and the determination of high risk or total number of deaths due to low doses is highly subjective and is expected to remain unknown [1]. The World Health Organization has estimated that over 40,000 cases of cancer are expected by 2065 due to the accident, of which over 16,000 cases are expected in Europe outside the contaminated areas. In 2020, Hauptmann and other 15 international researchers of eight Nations, among which: Institutes of Biostatistics, Registry Research, Centers of Cancer Epidemiology, Radiation Epidemiology, and then also U.S. National Cancer Institute (NCI), International Agency for Research on Cancer (IARC) and Radiation Effects Research Foundation of Hiroshima studied definitively through meta-analysis the damage resulting from the "low doses" that have afflicted the survivors of the explosions of the atomic bombs on Hiroshima and Nagasaki and also of accidents of nuclear plants that have occurred in the world. The scientists reported, in *JNCI Monographs: Epidemiological Studies of Low Dose Ionizing Radiation and Cancer Risk*, that the new epidemiological studies directly support excess cancer risks from low-dose ionizing radiation [2]. Only recently the World Health Organization has estimated that over 40,000 cases of cancer are expected by 2065 due to the accident, of which over 16,000 cases are expected in Europe outside the contaminated areas. In 1986, Russian epidemiologists increased the official number to 30, reflecting the deaths of 28 additional plant workers and first responders in the months after the accident. Thyroid cancer has been relatively amenable to treatment for several decades. But attributing a mortality rate of 1% to the 16,000 cases across Europe, as predicted by Tuttle and Cardis, the total death rate from radiation-induced thyroid cancer is expected to reach 160 [3, 4]. In 2022, Wojcik [5] reported that the 2021-UNSCEAR is the fourth report since 1994 affirming the linear non-threshold (LNT) dose response for low radiation-induced cancers. On the contrary, Katherine Harmon in "*Scientific American — Health — 2012*" wrote that some public health experts, agree that the radiation fears were overblown, and that other well-known researchers comparing with the effects of the radiation exposure from Fukushima, state that: "*in terms of the health impact, the radiation is negligible and heart disease and depression are likely to claim more lives than radiation after the earthquake, tsunami, and that the radiation will cause very few, close to no deaths.*" [6].

The Most Studied Radionuclides: Iodine-131, Cesium-137. The metabolism of radionuclides, such as cesium and iodine in biology, has been studied by many scientists, initially only to investigate the new radiation damage of atomic explosions after 1945. Only later researchers have investigated the role of these elements in biology and physiology. Among these researchers are Nelson et al. (1961) [7], Ullberg et al.

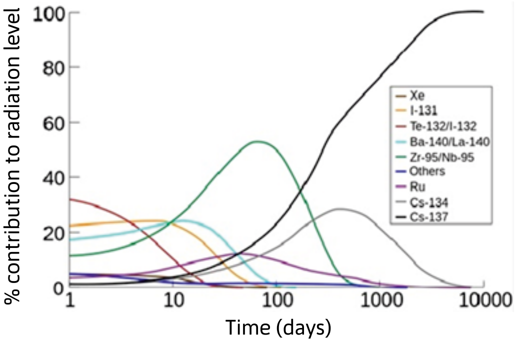

Figure 1. The relative contributions of the major nuclides to the radioactive contamination of the air after an accident. Retrieved on 2009 http:/atom.kaeri.re.kr

(1961) [8], Pellerin et al. (1961) [9], Rosoff et al. (1963) [10], Lestaevel et al. (2010) [11], and recently Venturi et al. (1985, 1999, 2011, 2020–2022) [12–17]. These radionuclides act also with low radiation doses which are much lower than the known rapidly lethal doses, however, they are very prolonged, even for years, the carcinogenic damage is detectable only with a stochastic analysis (on large numbers). The carcinogenic damage of DNA on one chromosome allele becomes evident only subsequently and may also occur after ten or more years, transforming the affected cell into a cancer cell.

Two different ways of bioaccumulation of radionuclides in the body are:

(1) high but single dose (e.g., 1000 Bq) bioaccumulation, or short half-life radionuclide (such as iodine-131, which has a half-life of 8 days);

(2) low but prolonged dose (e.g., 10 or 1 Bq/day), or long half-life radionuclide (such as cesium-137, with half-life = 30.2 years, or cesium-134, with half-life = 2 years).

According to the International Atomic Energy (IAEA) [18], the radioactivity, with consequent fallout, released into the atmosphere from nuclear weapons testing was far greater than that from nuclear accidents in power plants:

— 400 PBq from nuclear weapons testing
— 85 PBq from Chernobyl,
— 10–30 PBq from Fukushima.

Iodine-131 may give a higher initial dose, but its short half-life of 8 days ensures that it will soon be gone, remaining in the environment for approximately 100 days only. Cesium-137 decay by gamma and beta (electron) emissions produces highly ionizing radiation [10]. Beta emission is very dangerous when radio-Cs is ingested, because it deposits all energy in a very short distance of 3–4 mm (several hundred cells in pancreatic tissue). The International Commission on Radiological Protection (ICRP) sets radiation safety standards and recognizes that radio-Cs bioaccumulates harmfully in humans and in predatory animals. The reported ICRP compares single ingestion of 1000 Becquerel (Bq) of 137-Cs, a one-time exposure, with the daily ingestion of 10 Bq. On the single exposure, it is noticed that half of the 137-Cs has disappeared from the body in 110 days. That is considered to be the biological half-life. Note also that with the routine daily ingestion of 10 Bq of 137-Cs the total radioactivity within the body continues to rise until after about 500 days when there are more than 1400 Bq of radioactivity measured in the body [11]. The cumulative biological internal dose (and relative damage) is well represented by the attached graph, where the child is more affected and damaged than the adult.

Radio-Iodine. Absorption of radio-iodine (131-I) can lead to acute and chronic effects. Acute effects from high doses include thyroiditis, while chronic and delayed effects include hypothyroidism, thyroid nodules, a thyroid cancer (TC). It has been shown that 131-I released from Chernobyl caused an increase in the incidence of TC in the former Soviet Union and also in Fukushima, but TC mortality rates are generally low, even at higher tumor stages [3, 4]. 131-I may give a higher initial dose, but its short half-life of 8 days ensures that it will soon be gone. 131-I remains in the environment for about 100 days.

One measure, which protects against this risk, is taking a dose of potassium iodide (KI) before exposure to radioiodine. The non-radioactive iodide saturates the thyroid, causing less storage in the body, reducing its damage by 99% [19, 20]. Iodine is an essential trace element in biological systems. It is a component of biochemical pathways in organisms from all biological kingdoms, suggesting its fundamental significance throughout the evolutionary history of life [14]. Iodine is present in thyroid hormones: thyroxine (T4), which is converted to the active triiodothyronine (T3) within cells by deiodinases (5'-iodinase). These are further processed by decarboxylation and deiodination to produce iodothyronamine, thyronamine and free iodine. Iodine accounts for 65% of the molecular weight of T4 and 59% of T3. Indeed, the total amount of iodine in the human body is still controversial.

In 2001, M.T. Hays [21] reported in medical journal "*Thyroid*" that: "*it is surprising that the total iodine content of the human body remains uncertain after many years of interest in iodine metabolism*". Only thyroidal iodine content has been measured accurately and the estimate of 5–15 mg in the normal human thyroid is now well established. Hays reported that Salter [22], in 1940, quoted a figure of 10 to 50 mg for total body iodine; Sturm and Riggs, in 1952 [17], estimated normal thyroidal iodine to be 8 mg and other iodine pools to total 1.3 mg. Hamolsky [23], in 1965, estimated total body iodine to be 9–10 mg, of which 8 mg is in the thyroid gland. In 1967, Margaria [24], gave a figure of 50 mg for total human iodine content, as also, more recently, reported by Venturi [15, 25]. Margaria assigned 10–15 mg to the thyroid, 10 mg to the bones and muscles, 5 mg to the epidermis, and 15 mg to the salivary glands and gastric mucosa. In 1996, Delange [26] and Brown-Grant [27] estimated total body iodine to be 15–20 mg". Indeed only 10–15 mg of the total human body iodine (about 50 mg) is concentrated in thyroid tissue and its hormones, and, about 70% of all iodine in the body is found in other tissues, including mammary glands, eyes, gastric mucosa, fetal thymus, cerebro-spinal fluid (CSF) and choroid plexus, arterial walls, the cervix, germinal cells of ovary and testis, pancreas and salivary glands. In the cells of those tissues, iodide (I^-) enters directly by sodium-iodide symporter (NIS). It has been shown to have a suppressive effect on some cancerous cells. In 1985, Venturi first published in his Italian book [12] that iodide ion functions in these organs as an antioxidant reducing substance that detoxifies poisonous reactive oxygen species (ROS), such as hydrogen peroxide. All these iodine-capturing organs are damaged by radio-iodine in which it can trigger pathogenic and carcinogenic mechanisms. Furthermore, iodine deficiency is the main cause in the world of mental retardation.

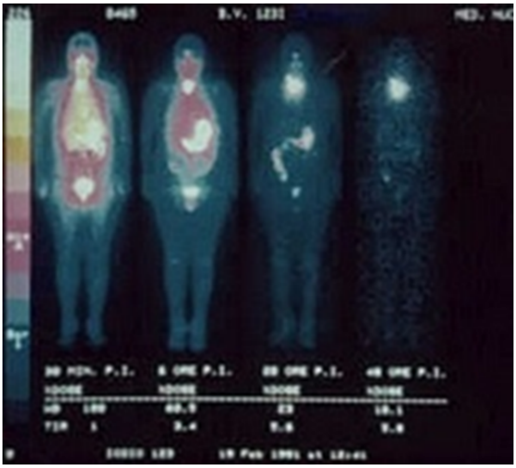

Figure 2. Sequence of 123-iodide human scintiscans after an intravenous injection, (from left) after 30 minutes, 20 hours, and 48 hours. A high and rapid concentration of radio-iodide is evident in extrathyroidal organs like cerebrospinal fluid (left), gastric and oral mucosa, salivary glands, arterial walls, ovary and thymus. In the thyroid gland, I-concentration is more progressive, as in a reservoir (from 1% after 30 minutes, and after 6, 20 h, to 5.8% after 48 hours, of the total injected dose [14].

Radio-Cesium. Radionuclide contamination in terrestrial ecosystems has reached a dangerous level. The major artificial radionuclide present in the environment is cesium-137 (137-Cs). In humans and animals, cesium ion (Cs^+) behaves like potassium ion (K^+). Cs is also ab-

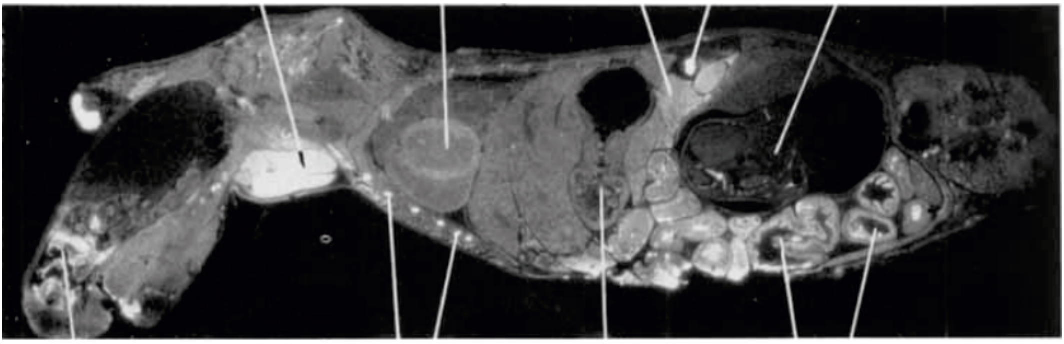

Figure 3. Autoradiogram showing 137-Cs distribution in a pregnant mouse 6 hours after intravenous injection. White areas correspond to high radioactivity. Uptake is high in the salivary gland, pancreas and intestine. In fetuses, concentration is significantly lower than in the mother. In the pancreas, the islets of Langerhans appear to have a slightly lower activity than the acinar tissue [7].

sorbed from plants and fruit competitively with K and is localized mainly inside the cells. Pancreas and salivary glands secrete Cs in the intestine thus eliminating about 14% of ingested Cs with the feces, the remaining 86% is eliminated by kidney with the urine. The Author reported the correlation between the geographical map of the incidence and mortality from PC and the map of nuclear plant accidents, atomic bomb testing and radioactive fallout [15, 16]. Worldwide death rate of PC is increasing, but the exact cause is still not known.

Ingested radio-cesium may also cause in humans several cases of pancreatitis with secondary pancreatogenic diabetes (type 3c), which are both on the rise in the world [16, 17]. The worldwide death rate of PC is increasing, but the exact cause is nowadays still not known. Published data in medical literature at World, European and Italian levels are reviewed and compared. 137-Cs, with a half-life of about 30 years, is still present in the environment for more than 300 years.

The data published in the international, European and Italian medical literature are reviewed and compared. 137-Cs remains in the environment for many years. Autoradiographic studies in mice have shown that 137-Cs is concentrated in greater quantity in the pancreas, particularly in exocrine cells, where most malignant PCs originate. Gemici et al. (2018) [28] have shown that, contrary to what was believed, the human pancreas has a high radio-sensitivity and becomes functionally insufficient with great volumetric loss in the irradiated patients of about 56%. Therefore, as it may happen accidentally during irradiation for stomach cancer, the mean dose of radiation on the behind pancreas should be kept below 20–25 Gray to preserve its functions. Nelson et al. [7] showed that 137-Cs is concentrated in larger quantity in pancreatic exocrine cells, where most PCs (about 90%) originate, and showed a non homogeneous selectivity for Cs in different organs. Children have shown absorption of radio-Cs and other radionuclides more than double that of adults. In autopsies of contaminated children, Bandazhevsky found a high accumulation of 137-Cs in the pancreas (and also in thyroid and adrenal glands) detecting levels up to 40–45 times higher than in the liver [29]. Bioaccumulation is the process through which radio-Cs accumulate and are stored more easily in living organisms than in the environment. The accumulated concentration of chemicals or radionuclides increases then more rapidly than their removal by excretion and metabolism. It is greater in carnivores than in herbivores. Venturi reported that in pancreatic gland radio-cesium can cause pancreatitis and cancer with damage of pancreatic islets with diabetes (type 3c) [13,14]. In fact, diabetes mellitus increased in contaminated population, particularly children and adolescents, following the Chernobyl and Fukushima [3, 4] nuclear incidents [30–33]. At the same time, worldwide pancreatic diseases, diabetes and environmental radio-cesium are also increasing. "*Prussian Blue*" (ferric ferrocyanide) is able to chelate Cs in the intestine and, preventing its reuptake, eliminates it with feces. Nielsen et al. [34] studied the effects of two Prussian blue derivatives on intestinal absorption of 134-Cs in two male volunteers. Their results indicated that administration of this substance (0.5 g) simultaneously with the test-meal decreased 134-Cs uptake to approximately 50%, and that the daily administration of 0.5 g × 3 decreased the elimination half time of previously absorbed 134-Cs from about 100 to about 50 days. Melo et al. [35, 36] reports that in case of strong accidental ingestion of radio-Cs the chelating action is recommended.

Pancreatic Cancer in the World and in Europe. In the early 1970's, mortality from PC was low in Europe, stomach cancer being among the leading causes of cancer death [1, 37, 38]. Nowadays, after about 50 years, the trends of these cancers are reversing. As the probable cancer latency is about 8–10 or more years. There was a relationship between the PC and the radioactive fallouts of the numerous atomic bomb testing carried out mainly in the years 1960–1970 and nuclear power plant accidents. Thyroid and pancreatic cancer increase begins in the early 1980s and, in Europe, after the 1986 Chernobyl accident. The incidence of PC varies across regions and populations. In 2018, 458,918 new cases of PC were registered worldwide, accounting for 2.5% of all cancers. The age-standardized rate (ASR) incidence was very high in Europe (7.7 per 100,000 people) and North America (7.6 per 100,000 people), followed by Oceania (6.4 per 100,000 people). The lowest rate was observed in Africa with an estimated incidence of 2.2 per 100,000 people [16, 24]. Differences in incidence rates were 30 times greater among the populations with the highest rate (Hungary: 10.8), and the lowest rate (Guinea: 0.35) [39]. Recently, Uccelli et al. (2021) reported that in Italy the incidence of PC is growing significantly (+ 0.4% annually), with a great North-to-South gradient: compared with northern Italy, in central Italy PC incidence levels are 29% lower in males and 26% lower in females, and in southern Italy, they are 25% and 28% lower respectively. PC ranking among the causes of death due to tumors is 4th in females, total (M + F) PC mortality being 6 %. These data are related to the current exposure to 137-Cs in Italy [40]. The radioactive cloud of Chernobyl also hit the northern part more because the radioactive cloud came from Northern Europe and covered about half of Italy, while southern Italy was almost completely untouched.

Pancreatic Cancer in Japan. In Japan, PC is the fourth leading cause of cancer deaths. It is an aggressive disease where approximately 60%–80% of patients already have distant metastasis at presentation with a poor survival rate, especially after the nuclear accident of Fukushima, the PC has an unusually high frequency. The Japanese "*Global Data*" in 2019 predicted that this cancer will continue to increase in Japan in the next ten years, despite the decrease in the Japanese population. Epidemiologists predict an increase in cases from 42,000 cases in 2019 to 48,000 cases in 2029, with an annual growth rate (AGR) of 1.50%. The incidence of PC in Japan has increased continuously especially in the last decades. The rate of incidence in 2019 was almost double that of the US and about 50% higher than that of France, Germany, Italy, Spain and the United Kingdom. This trend is likely to continue in the next decades. According to Japanese researchers the cause of this increase is unknown, in fact while smoking, old age and obesity are the main risk factors, the Japanese population has not greater risk of obesity and smoking-related diseases compared to other nations. In addition, Japan has an aging population, and is susceptible to this type of cancer, similar to that of the aforementioned European nations (2020) [30, 31], Japan has an exceptionally high burden of PC. Epidemiologists forecast that this cancer burden will continue to rise in Japan in the next ten years despite the decrease in the Japanese population and forecast an increase in diagnosed incident cases of PC in Japan from 42,000 cases in 2019 to 48,000 cases in 2029, at an annual growth rate (AGR) of 1.50%. Prior to the Tōhoku earthquake and tsunami in 2011, Japan had generated 30% of its electrical power from nuclear reactors and planned to increase that share to 40%. As of March 2020, out of the 54 nuclear reactors, there were 42 operable reactors but only 9 reactors in 5 power plants were actually operating [42]. The areas where both PC rates and nuclear power production are high often coincide. Higher levels of nuclear power production are subject to higher risks of accidents. Chernobyl was the most serious nuclear accident in the history of nuclear power plants [43]. But many other minor accidents occurred in various countries which have not been reported.

Conclusion. New metabolic pathways of radionuclides in animal and human organism are reported. Stochastic analysis of tumor epidemiology may be key to interpreting the etiology of cancer and of some inflammatory diseases and also of diabetes mellitus, which are on the rise in the world [16], and therefore, the cornerstone for developing a possible prevention strategy. The reported data support investigations into an association between radio-iodine and radio-cesium and cancer. If this correlation is confirmed, a preventive action may be possible by using iodized table salt also enriched in potassium and by a diet with marine food and fruits and vegetables, rich in iodine and in potassium. Food must also come from areas not contaminated by radioactivity. Fossil oil will likely run out within the next 50–80 years. Alternative energies: sun, wind, hydro, tides, etc. will probably not be able to provide us with the amount of energy needed for a world population, which may be as high as ten billion. All this might cause hunger, poverty, wars, dictatorships, etc. Which energy can we use and at which risk?

I hope that this research will help to defend, in part, world population from the worrying risks of nuclear fission.

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