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ЗАБОЛЕВАЕМОСТЬ ЖИТЕЛЕЙ БЕЛАРУСИ, ОБЛУЧЕННЫХ I-131 ВО ВРЕМЯ ВНУТРИУТРОБНОГО РАЗВИТИЯ В РЕЗУЛЬТАТЕ АВАРИИ НА ЧЕРНОБЫЛЬСКОЙ АЭС

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При анализе когорты индивидуумов, проживающих в Столинском р-не Брестской обл., которые получили облучение при внутриутробном развитии за счет накопления I-131 в щитовидной железе, было обнаружено, что как общая заболеваемость, так и заболеваемость нервной, сердечно-сосудистой, мочеполовой систем, а также желудочно-кишечного тракта повышена и отличается в значительной степени от заболеваемости индивидуумов, идентичных по ряду параметров, которые не подвергались *in utero* воздействию радиоактивного йода. В исследуемой выборке преобладали относительно небольшие дозы, не превышающие 30 мГр. И лишь у 10 % облученных дозы составляли около 100 мГр. В группе облученных I-131 *in utero* детей в последующие годы наблюдается линейная частота заболеваемости психическим расстройством и расстройством поведения (класс V по МКБ-10), которая почти в три раза больше, чем в группе необлученных индивидуумов. Примерно такую же зависимость можно наблюдать по группе заболеваний нервной системы (класс VI). Частота сердечно-сосудистой патологии в основной группе была примерно в 2,5 раза больше, чем в контрольной. В выборке детей, которые подвергались действию I-131 во внутриутробном состоянии, заболеваемость болезнями мочеполовой системы (класс XIV) регистрировалась на протяжении всего периода наблюдения, то есть до 2017 г. и была повышенной примерно в 4 раза. Появление патологии носило отсроченный характер, проявляющееся спустя 10 лет после аварии на ЧАЭС. В большинстве случаев заболеваемость в группе необлученных лиц имело сигмоидную зависимость и выходило на плато, в дальнейшем не увеличиваясь. Напротив, в группе облученных пострадавших заболеваемость имела тенденцию к росту. Наблюдаемые данные могут быть вызваны вариабельной чувствительностью определенных генов ткани щитовидной железы, которые получают лабильность, что приводит к измененному гормональному фону тиреоидных гормонов, которые воздействуют на все без исключения системы организма, приводя впоследствии к появлению патологии.

Ключевые слова: радиоактивный йод, I-131; заболеваемость; нервная система; сердечно-сосудистая система; мочеполовая система; желудочно-кишечный тракт; щитовидная железа; тиреоидные гормоны.

ANALYSIS OF THE MORBIDITY OF RESIDENTS OF BELARUS WHO RECEIVED THYROID EXPOSURE DUE TO THE ACCUMULATION OF I-131 DURING FETAL DEVELOPMENT AS A RESULT OF THE ACCIDENT AT THE CHERNOBYL NUCLEAR POWER PLANT

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Analysis of the cohort of individuals living in the Stolin district of the Brest region, who received exposure during prenatal development due to the accumulation of I-131 in the thyroid gland, has shown that both the general morbidity and the morbidity of the nervous, cardiovascular, genitourinary systems, and also of the gastrointestinal tract, are increased and differs from the incidence in individuals, identical in a number of parameters, who were not exposed to radioactive iodine *in utero.* The study cohort was dominated by relatively small doses to the thyroid gland, not exceeding 30 mGy. And only 10 % of the irradiated doses were about 100 mGy. In the group of children irradiated *in utero* with I-131 in subsequent years, a linear incidence rate for mental and behavioral disorders (Chapter V according to ICD-10) is observed, which is almost three times higher than in the group of non-irradiated individuals. Approximately the same dependence can be observed in the group of diseases of the nervous system (Chapter VI). The frequency of diseases of the circulatory system (Chapter IX) in the main group was approximately 2.5 times higher than in the control group. In a cohort of children who were exposed to I-131 in utero, the incidence of diseases of the genitourinary system (Chapter XIV) was noted throughout the entire observation period, i.e. until 2017 and was increased by about 4 times. The appearance of the pathology was delayed, and it has started to manifest 10 years after the Chernobyl accident. In most cases, the incidence in the group of non-exposed persons had a sigmoid dependence and reached a plateau without further increase. In contrast, in the group of exposed victims, the incidence tends to increase. The observed data may be explained by the variable sensitivity of certain genes of the thyroid tissue to radiation. They might become up- or downregulated and lead to an altered thyroid hormone background, which affected all body systems without exception, subsequently causing the appearance of multiple pathology.

Keywords: I-131; morbidity; incidence; nervous system; cardiovascular system; genitourinary systems; gastrointestinal tract; thyroid.

Introduction

It is known that radiation accidents at nuclear fuel cycle enterprises are accompanied by the release of uranium fission products, including iodine isotopes, into the environment. I-131 is dominant among them. This product accumulates mainly in the thyroid gland (TG), which leads to its exposure. Earlier, we studied a cohort of women living in the Stolin district of the Brest region, who at various stages of pregnancy at the end of April 1986 fell under a radioactive cloud containing iodine isotopes because of the accident at the Chernobyl nuclear power plant (ChNPP). The incidence of their pathology was studied over the next 30 years [1]. It was found that after a rather long period of time they had an increased incidence of cardiovascular pathology and pathology of the respiratory system, compared with the control group, who were pregnant later, after the breakdown of I-131 [2]. Cardiovascular pathology was represented mainly by primary hypertension [3]. At the same time, both essential hypertension and respiratory diseases were characterized by the dependence on the absorbed dose by the thyroid gland of women.

The analysis of the state of health of children born by those women is of an undoubted interest. The fact is that in addition to the neuro-hormonal and other relationships between the body of a woman and the fetus, one should consider the incorporation of radioactive iodine in the fetal thyroid gland because of its accumulation due to the passing of the transplacental barrier [4]. This accumulation led to the formation of a determined absorbed dose. It is known that the thyroid gland performs very important functions, regulating, among other things, the basic metabolism in the body and so the development of the organism itself. In this regard, it is of interest to analyze the health status of individuals who have received exposure to I-131 in utero.

We have been able to trace the relationship of women exposed as a result of the accident at the ChNPP with the children they gave birth to for three decades. Accordingly, the aim of the present study was to analyze the incidence of different pathologies in persons exposed during fetal development in comparison with a cohort of individuals who were born later, when I-131 had practically completely decayed.

Materials and methods

As the main group of individuals, residents of the Stolin district of the Brest region were taken, who were born by women who lived there in late April-early May 1986 and were affected by a radioactive cloud that passed through this region of Belarus. The cloud contained iodine radionuclides, including I-131. It entered the body of women by inhalation, orally with food, and also through the skin. Once inside the body, it was distributed, accumulated in the thyroid gland and entered the fetal body through the transplacental barrier, concentrating in its thyroid gland. The main cohort included 123 individuals, including 62 women and 61 men. Dates of birth were in the range of 06/03/1986-02/06/1987. The average value of the absorbed dose by the thyroid gland was 32.2±3.31, median 22 mGy, in males – 35.4±5.4, median 23 mGy, in females – 29.1±3.9, median 22 mGy.

When analyzing the effects of radiation on certain segments of the population, it is always necessary to have a comparison group consisting of individuals who have not received exposure. In this study, the comparison group also included residents of the Stolin district of the Brest region, but they were born later. In other words, mothers of persons from the control group did not receive radioactive «iodine shock». Control group included 113 individuals from the same region, identical not only in terms of residence, but also in social status: 57 of them were males and 56 of them were females. Their dates of birth were in the range of 01/03/1988–12/31/1988. The comparison group was selected taking into account the half-life of

I-131, which is about 8 days. For 10 half-lives, i. e. after 80 days, only trace activities of radioactive iodine remained in the medium and, consequently, the mothers of these children did not receive thyroid exposure during pregnancy.

Verified data on the state of health of exposed and non-exposed individuals were obtained from the State Register of Persons Affected by the Chernobyl Accident. Only primary morbidity was taken into account in the work.

Absorbed doses by the thyroid gland due to I-131 incorporation were calculated by the head of the laboratory for the reconstruction of exposure doses to the population of the State Scientific Center of the Federal Medical Biophysical Center A.I. named after Burnazyan FMBA of Russia, Doctor of Technical Sciences, S. M. Shinkarev. Doses were calculated using a semi-empirical model from the 2004 year iteration.

Statistical data processing was carried out using Statistics 10.0 (StatSoft. Inc., USA) and SigmaPlot 12.5 (Systat Software Inc., Germany).

This study was approved by the Ethics Commission of the Belarusian Association of Physicians (10.12.2020).

Results and discussion

First of all, it is necessary to assess the impact of radiation on children exposed in utero. Figure 1 shows a diagram of the distribution of absorbed doses on the thyroid gland of the mentioned children. Obviously, relatively small doses, that do not exceed 30 mGy, dominate there. And only 10 % of those doses were about 100 mGy.

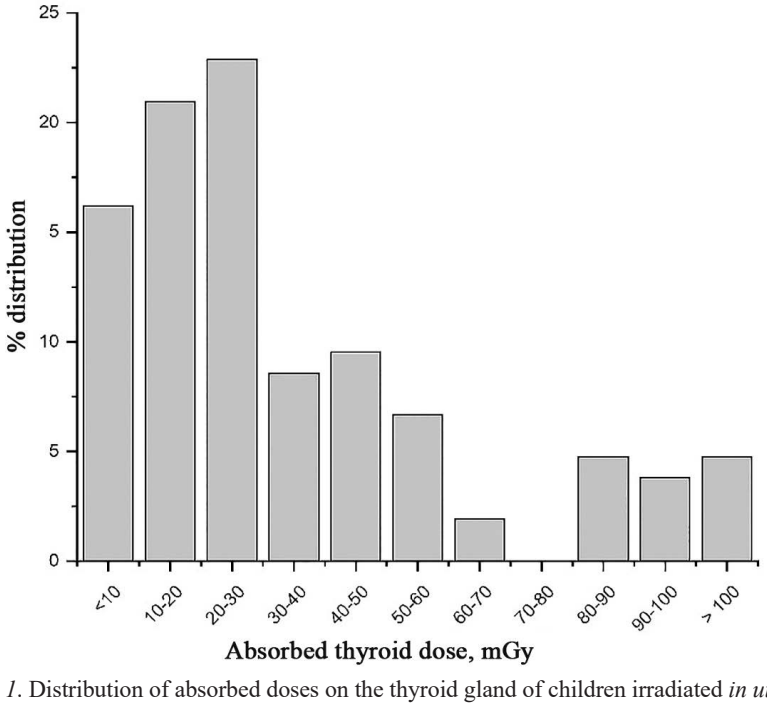

Fig. 1. Distribution of absorbed doses on the thyroid gland of children irradiated *in utero*

Fig. 2 shows the total cumulative incidence of pathology for exposed and non-exposed individuals. According to the search for mathematical dependencies and coefficients of determination (COD), the incidence in both cases is described by a sigmoid curve. It is clearly seen that the dynamics of the general morbidity in irradiated individuals differs from that characteristic of individuals who were not irradiated in 1986. For the first of them, the cumulative curve grows more or less evenly upwards. While in non-irradiated females and males, it reaches a plateau after 2000. Surprisingly, the sharper increase in incidence in the group of non-exposed individuals in 1996–2000 has been observed. An analysis of this phenomenon revealed that this rise is due to a large contribution of respiratory organs pathology to the common incidence (32 % vs. 13 % non-exposed). In other words, this rise was caused by a pathology of an infectious nature (flu, acute respiratory infections). Paradoxically, individuals irradiated in utero appeared to be more resistant to these diseases.

Consideration of gender differences in general morbidity showed that in the group of residents of the Stolin district exposed in utero, the nature of the manifestation differs in females and males. If in the group of girls exposed in utero, the incidence is characterized by a linear dependence, then in boys there is a sigmoid curve with a gradual decrease in the frequency of the pathology (Fig. 3). The cumulative morbidity of non-irradiated children of both sexes repeats the relationship shown in Fig. 2. The sigmoid curves are characterized by a sharp rise in the 1986–2000 period and they are almost overlapped with each other (Fig. 4). The sharp rise in incidence in this group has already been discussed. It is caused by a pathology of respiratory system of the infectious

nature. However, the cumulative incidence in the main group in 2016 is significantly higher than in the cohort of unexposed individuals.

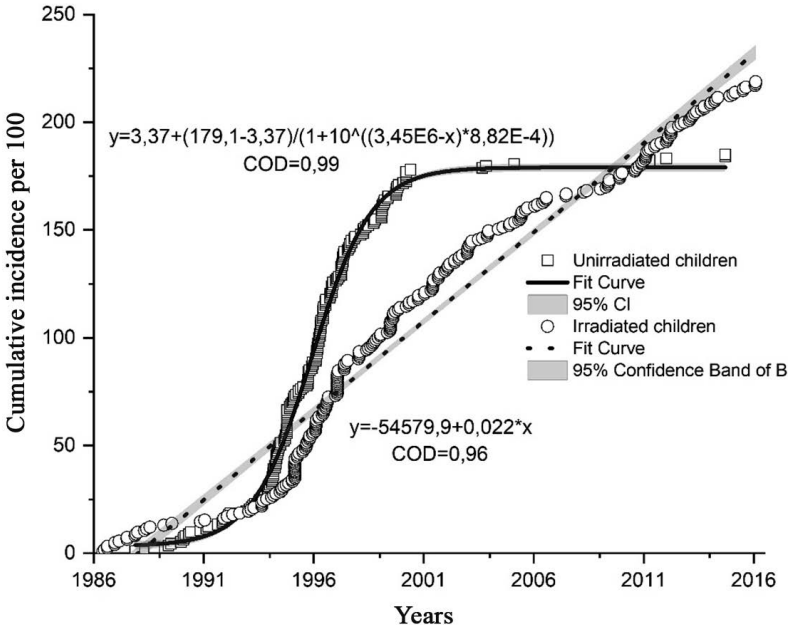

Fig. 2. Cumulative incidence for all classes of pathology in irradiated and non-irradiated individuals

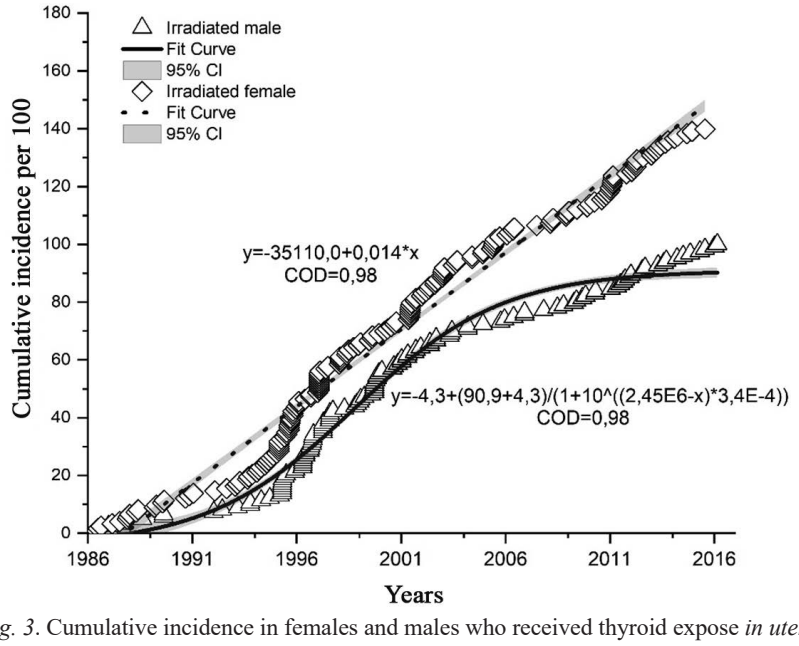

Fig. 3. Cumulative incidence in females and males who received thyroid expose *in utero*

Even more striking results were found after the analysis of different classes of diseases in the two study groups. This is especially noticeable when comparing the incidence of mental and behavioral disorders (Chapter V according ICD-10) (Fig. 5).

In the group of children irradiated in utero with I-131, in subsequent years a linear incidence rate is observed, which is almost three times higher than in the group of non-irradiated individuals. Moreover, in the latter, the incidence rate after 2001 year tends to form a plateau.

Approximately the same dependence can be observed in the group of diseases of the nervous system (Chapter VI) (Fig. 6). The incidence in the main group was significantly higher, and in the control group it tended to stabilize.

A similar character of the curves was noted in the group of diseases of the circulatory system (Chapter IX) (Fig. 7). In both cases, the approximation curves had an S-shaped character, but they reached a plateau at different time intervals: the cumulative morbidity curve in the group of those exposed in utero seems to stabilize after 2006,

while the morbidity curve in the control group reached a plateau after the year of 1993. The incidence rate in the main group was approximately 2.5 times higher than in the control group.

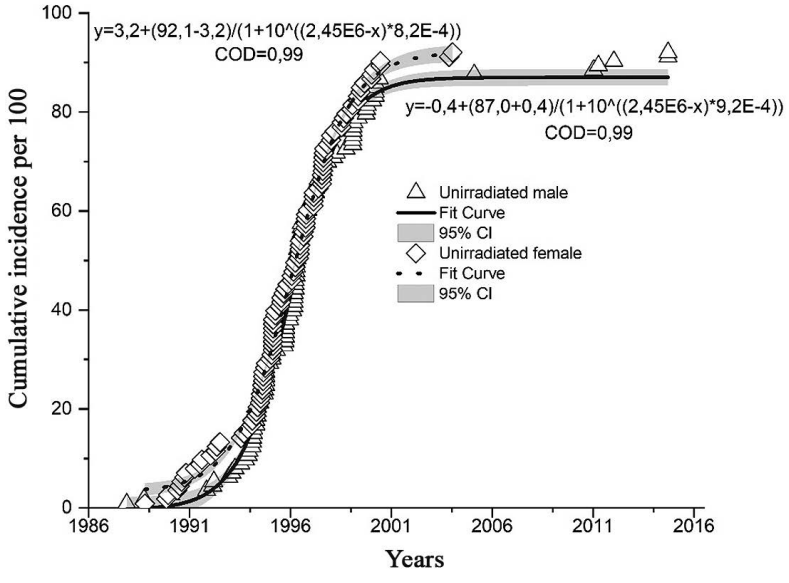

Fig. 4. Cumulative incidence in females and males who were not exposed to radioactive iodine

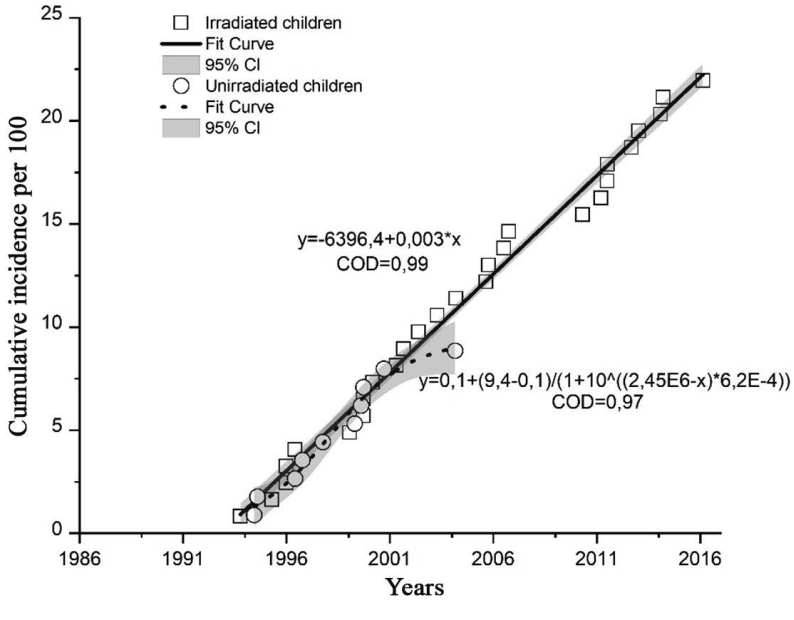

Fig. 5. Cumulative incidence of mental and behavioral disorders (Chapter V) in the group of exposed and non-exposed individuals

Interesting results were obtained after the analysis of morbidity in both cohorts for the group of diseases of the digestive system (Chapter XI) (Fig. 8). Morbidity in the group of residents of the Stolin region who were not exposed to irradiation of thyroid glands increased dramatically between 1995 and 2000. The morbidity curve of those exposed in utero was flatter and was characterized by a lower level of registration of this pathology. Among the latter, diseases of the stomach (gastritis), duodenum (duodenitis) and pathology of the biliary tract were recorded. It is rather difficult to explain this phenomenon.

The incidence of diseases of the genitourinary system (Chapter XIV) is shown in Fig. 9. Obviously, in the group of non-irradiated individuals, cases of this pathology were registered at the end of the 90s of the previous century. Later cases of morbidity were not recorded. On the other hand, in a cohort of children who were exposed to I-131 in utero, the incidence was recorded throughout the entire observation period (i.e. until 2017) and increased about 4 times.

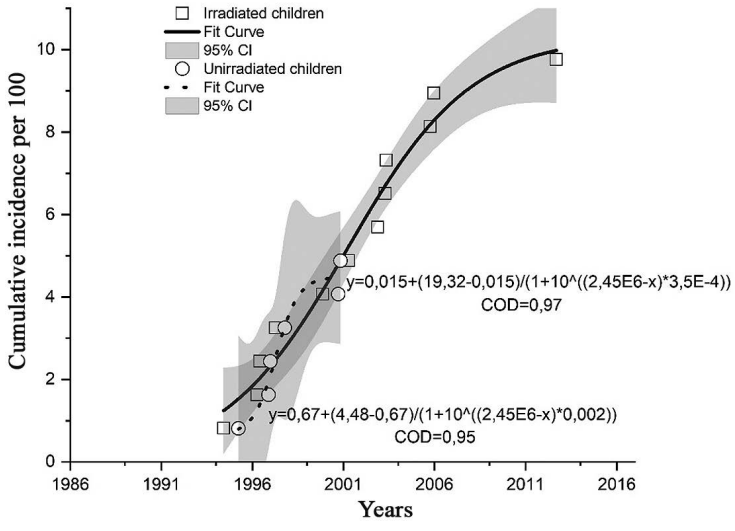

Fig. 6. Cumulative incidence of diseases of the nervous system (Chapter VI) in a group of exposed and non-exposed individuals

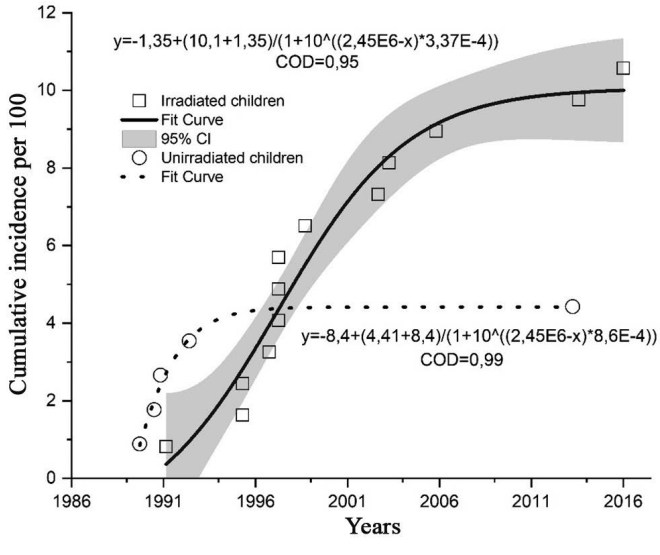

Fig. 7. Cumulative incidence of diseases of the circulatory system (Chapter IX) in the group of exposed and non-exposed individuals

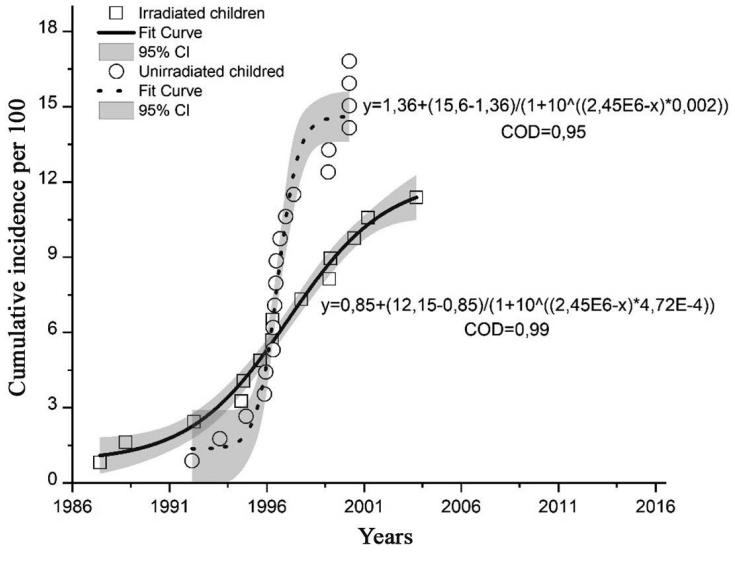

Fig. 8. Cumulative incidence of diseases of the digestive system (Chapter XI) in the group of exposed and non-exposed individuals

After the analysis of the presented results it became obvious that intrauterine irradiation of the thyroid gland with radioactive iodine, without any doubt, changed the morbidity of affected individuals in the future. This applies both to general morbidity and pathology of the nervous, cardiovascular, digestive and urinary-genital systems. Previously, we have already described changes in the incidence of primary hypertension in women who, during pregnancy, were exposed to I-131 released during the Chernobyl accident. The phenomenon was dose-dependent and did not appear immediately, but 15 or even 28 years after exposure. We explained this fact by the variable activity of genes under the action of radioactive iodine [3], their subsequent instability, and the close relationship between thyroid hormonal activity and the function of the cardiovascular system.

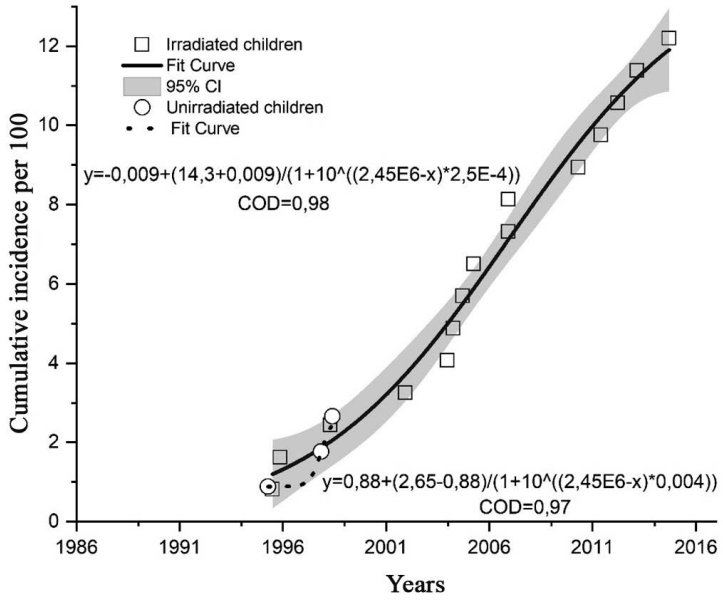

Fig. 9. Cumulative incidence of diseases of the genitourinary system (Chapter XIV) in the group of exposed and non-exposed individuals

Approximately the same data with morbidity maxima were found in relation to cerebrovascular pathology in victims who received radiation from radioactive iodine [5]. The maximum of this pathology was recorded in approximately the same range (12-21 years), but as a result of exposure to large absorbed doses.

The explanation of changes in morbidity in relation to the pathology of the nervous, digestive and genitourinary systems is more difficult. Thyroid hormones (3',5',3,5-L-tetraiodothyronine (T4), 3',5,3-L-triiodothyronine (T3), 3',5', 3-L-triiodothyronine (rT3) and 3 ,5',-L-diyothyronine (3,5-T2) are involved in the development and functioning of the most of organs and systems of the body [6]. It is known that during the first trimester of pregnancy, the developing fetus needs maternal thyroid hormones (thyroxine, triiodothyronine) [7] Moreover, thyroid hormones have been shown to play an important role in the prenatal and postnatal development of the nervous system and are involved in several processes such as neurogenesis, gliogenesis, myelination, synaptogenesis, etc. [8]. Decrease in thyroxine level in the mother in the first trimester of pregnancy, regardless of whether it is accompanied by an increase in the level of thyroid-stimulating hormone, can lead to irreversible mental and psychomotor disorders. It has already been pointed out that certain thyroid genes can respond differently to radiation exposure due to the incorporation of I-131 [9]. It is quite possible that this mechanism may be responsible for the increased incidence in the main group in relation to diseases of the nervous system, as well as mental and behavioral disorders. In other words, the decrease in thyroxin during the in utero development may be associated with the subsequent appearance of mental pathologies, which we observe.

Interpretation of changes in the incidence of the digestive system pathology is quite difficult due to the paucity and contradictive nature of publications on the effect of the thyroid gland pathology on the development of gastrointestinal tract diseases. Thyroid hormones play an important role in the development of the gastrointestinal tract [10; 11; 12]. There is the evidence of the effect of a deficiency or excess of thyroid hormone production on intestinal motility, as well as on microscopic lesions of its epithelial layer [13; 14]. Thyroid hormones play an important role in the functioning of the liver [15]. Changes in their production level, from our point of view, can serve as the basis for the development of pathology in the long term.

There is much more research on the relationship between thyroid gland pathology and diseases of the genitourinary system. It has been established that thyroid hormones affect both the development and function of the kidneys [16; 17] causing changes in both glomerular filtration and mineral metabolism [18]. Thyroid dysfunction causes marked changes in glomerular and tubular functions, electrolyte and water homeostasis [19]. Therefore, the

instability of the genome occurred after radiation exposure, as well as the variability of thyroid genes expression after the accumulation of I-131 in it, can explain the data described above. The altered function of the TG may be the cause of the change in morbidity in the group of individuals affected in 1986.

Conclusion

The incidence of pathology, both the general one and for individual organs and systems (nervous, cardiovascular, digestive tract, genitourinary systems), is significantly increased in the group of individuals who, during fetal development, received thyroid irradiation due to transplacental intake of radioactive iodine from their mothers because of the accident at the ChNPP. Their incidence of pathology is progressive, in contrast to the incidence for non-irradiated persons, which stabilized over time. This may be due to the effect of I-131 on the genome of thyrocytes, leading to altered thyroid regulation of various organs and systems of the body.

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