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EPIDEMIOLOGICAL CHARACTERISTIC OF THE PROCEDURE OF FIRST SCREENING EXAMINATION OF STUDY SUBJECTS OF THE JOINT SCIENTIFIC UKRAINE-USA THYROID PROJECT

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В 1998 году начато выполнение совместного украинско-американского тиреоидного проекта “Научный проект изучения рака и других заболеваний щитовидной железы в Украине в результате аварии на Чернобыльской АЭС”, который предполагает обследование жителей Украины, пострадавших в результате аварии на Чернобыльской АЭС. Описана процедура регистрации учасиников проекта, клинико-лабораторного обследования и опроса с целью реконструкции дозы облучения щитовидной железы.

Ключевые слова: Чернобыльская катастрофа, Украинско-Американский Тиреоидный Проект, первое скрининговое обследование

Introduction

On April 26, 1986, during the accident at the reactor No 4 of the Chornobyl Nuclear Power Plant were released large quantities of radioactive iodine that accumulated intensively in thyroid gland, and may lead to functional disturbances of the gland. The estimate of biological risk from iodine radioisotopes is of paramount importance to the Public Health because the use of iodine-131 for therapeutic purposes continues and because radioisotopes of iodine represent a large part in the composition of radionuclides released during nuclear accidents or nuclear tests.

In order to settle these matters, long term epidemiological studies are being used that were actively conducted on contaminated areas of Belarus, Russia, and Ukraine [1, 2].

The biggest scale epidemiological (cohort) studies of thyroid pathology following the accident at the Chernobyl NPP – both by the size of study area and the number of study subjects – are interrelated Belarus-U.S. and Ukraine-U.S. Thyroid Projects [3].

To facilitate the investigation of the medico-biological effects of ionizing radiation during the Chornobyl accident in Ukraine, large-scale epidemiological studies have been planned in the framework of the “Scientific protocol for the study of thyroid cancer and other thyroid diseases in Ukraine following the Chornobyl accident”. Detailed information on the collaborative Ukraine-USA Thyroid Project, the procedure of establishment of the cohort of potential study subjects, identification of their current permanent address or place of provisional stay, invitation to the first screening examination, as well as the reasons of non-attendance or refusal – of part of the subjects – to participate in the screening, were the subject of a previous publication [4].

Study protocol

Protocol of the Ukraine-U.S. Thyroid Project “Scientific protocol for the study of thyroid cancer and other thyroid diseases in Ukraine following the Chornobyl accident” has been signed by Ukrainian and American collaborators in 1995. This document reflects scientific background and goals of the Study, outlines and explains selection of study areas and cohort, discuses study methods to be used and contains key aspects of Project implementation. Study Protocol is main referral document for all Project’s investigators, it served as a base for development of Study Manual of Operations.

Standartization of procedure of screening of study subjects

The procedure of screening of study subjects was standard, owing to a special Manual of Operations, which describes in detail all the aspects of medical screening, and owing to the use of standard Forms and Questionnaires during examination.

Manual of Operations

The aim of the Manual of Operations was to ensure documenting of all of the study procedures. This Manual was designed so as to allow all Project Investigators to use this Manual as an information source. The Manual is structured so that any Project Investigator may easily identify the chapters which describe the procedures necessary to carry out a specific task. The Manual of Operations of the Project consists of 9 chapters: "Introduction to the study", "Aim and structure", "Definition of study cohort", "Procedures of initial contact with study subjects", "Examination", "Laboratory examinations", "Final endocrine summary and recommendations", "Final diagnosis and cohort follow-up", and "Data management".

The addendum to the Manual of Operations contains data collection forms with instructions for their use, as well as models of other study documents (in particular, contact initiation letters, registration logs, management forms, reports, etc.).

Project's Structural subdivisions and their interaction

To ensure successful Project implementation, the following disciplinary areas of the Project have been organized – out of the staff of the V. P. Komisarenko Institute of Endocrinology and Metabolism, Academy of Medical Sciences of Ukraine, collaborators of the Center for Radiation Medicine, Academy of Medical Sciences of Ukraine, and local medical staff of Territorial Medical Sectors of eight districts – controlled by the Project protocol – of Zhytomyr, Kyiv, and Chernihiv regions: Project's Administration, Data Coordinating Center, Data Processing Center, Epidemiology Group (supported by local medical staff of eight study districts), Clinical group, Central Laboratory, Laboratory of Cytology, Laboratory of Pathomorphology, and Dosimetry Group.

The Data Coordinating Center ensures functioning of the Project central database, coordinates interaction of different areas of the Project, supports the main information flows between Project's investigators, develops specialized software for automation of individual processes, carries our key-entry of screening logs and part of clinical Forms directly to the Project's database, creates and supports analytical databases of the Project, which are used for efficient Project management, preparation of reports and scientific publications.

The Data Processing Center whose functions are fulfilled by the Louise Hamilton Kyiv Data Management Center of the University of Illinois at Chicago, ensures key-entering of complete sets of screening forms, registration of errors in form completion, develops recommendations for minimizing errors in entering primary information into screening forms and for improvement of quality control procedures.

The Epidemiology Group performs tracing and identification of study subjects' location; ensures invitation of potential study subjects to screening; works with those subjects who have not responded to invitation or relocated; coordinates activities with medical staff of districts controlled by the Project protocol; promotes participation of study subjects with detected thyroid abnormalities in follow up medical examinations at the Institute; collects information on hospitalization events and lethal cases among study subjects; takes part in data analysis, preparation of reports, etc.

Clinical group consists of medical teams (one fixed and four mobile teams) and experts-clinicians. Medical teams perform main, extra, and deepened examination of study subjects. The experts-clinicians ensures control of previous diagnoses, performs in-depth examination of study subjects with thyroid pathology, completion of forms "Final endocrine summary" with complex diagnoses, develops clinical criteria for all types of thyroid pathology taking into consideration

cohort's peculiarities, and carries out expertise of scientific publications with the results of Project implementation.

The Central Laboratory performs hormonal asseys, determines iodine excretion in study subjects.

The Laboratory of Cytology carries out a cytology study of specimens obtained by fine-needle aspiration biopsy of thyroid gland of study subjects, and provides cytology conclusions.

The Laboratory of Pathomorphology carries out intraoperative express-diagnosis of thyroid tumors, postoperative histological diagnosis of thyroid pathology, pathomorphological characterization and analysis of thyroid tumors of study subjects.

The Dosimetry Group summarizes available radioecological information necessary for dosimetry calculations, develops a detailed individual dosimetry Questionnaire, carries out interviewing and assembles an appropriate database of the results of interviewing, develops dosimetry models for calculation of in dividual dose estimates and their uncertainties, and uses these models for calculation of individual thyroid exposure doses for every study subjects.

Main stages of examination of study subject

According to the Project protocol, every study subject will have screening examination by a fixed team at the Institute of Endocrinology and Metabolism of the Academy of Medical Sciences of Ukraine, or by mobile teams (consisting of Institute's staff) visiting the subjects' local area (home hospital, polyclinic, out-patient clinic, or post of obstetric aid). Before the first examination, each study subjects was instructed about the purposes and tasks of the Project, after which a written consent to participate in the Project was obtained from each adult subject or from the parents of those study subjects who had not reached the age of 16 at the time of first screening examination.

Screening examination of study subjects includes registration, blood collection for further determination of thyrotropin stimulating hormone, free thyroxin (only in subjects with abnormal thyrotropic hormone level), thyroglobulin, antibodies to thyroid peroxidase and thyroglobulin, ionized calcium and parathyroid hormone (only in subjects with abnormal ionized calcium level), urine collection for further determination of urinary iodine level, palpation and ultrasound examination of the thyroid by an ultrasonographer, as well as thyroid palpation and clinical examination by an endocrinologist. All study subjects who were aged 10 years or more, or the parents of those study subjects who were aged under 10 years at the time of the accident, are given an interview in order to ascertain their relocation history, lifestyle, and nutrition peculiarities, as well as possible iodine prophylaxis after the accident – in order to reconstruct the thyroid exposure doses. The medical team's registrar received from the potential study subject a written informed consent, as well as detailed data concerning the place of residence of the study subject and of his (her) close relatives, marital status, education, kind of work, etc. The ultrasonographer performed thyroid palpation and thyroid ultrasound examinations of the study subject, and the results were recorded on magnetic medium. The endocrinologist collected the medical history (in particular, taking of medical preparations and dietary iodine consumption) and asked the study subject about symptoms characteristic of functional thyroid disorders, then he performed thyroid palpation and compared its results with those obtained by the ultrasonographer. In case of substantial discrepancies, both specialists perform a repeat examination and discuss the case so as to reach a consensus. Based on the results of ultrasound examination of the thyroid and personal examination, the endocrinologist completes a preliminary endocrine summary that comprises a preliminary diagnosis and recommendations concerning a possible follow up examination. So, in case of detecting some abnormalities (in particular, increased size, heterogeneous echostructure, or presence of nodular lesions in the gland) the subject was referred for an additional examination at the Clinic of the

Institute of Endocrinology and Metabolism (in particular, fine-needle aspiration biopsy of the thyroid), and appropriate treatment, if necessary. Criteria for referral and follow up examination described in the special sections of the Manual of Operations.

After obtaining, from the Institute's Clinical Laboratory, blood examination results (thyrotropin stimulating hormone, free thyroxine, antibodies, thyroglobulin, and ionized calcium levels), and, in case of need, the results of the additional examination, the endocrinologist establishes the final diagnosis for each study subject. Then the endocrinologist completes the final endocrine summary, which includes passport data on the study subject, results of blood tests, the results of ultrasound examination of the thyroid, diagnosis, and recommendations. The study subject may be recommended to attend for the following regular examination in 2 years (in the absence of thyroid pathology or in case of grade 1 diffuse goiter), to urgently have fine-needle aspiration biopsy of the thyroid or thyroid surgery (in case of nodular lesions detected in the thyroid), or to come to the Institute of Endocrinology and Metabolism for a follow up examination in the framework of the Project in 3, 6, or 12 months (in case of abnormalities of thyroid structure or function). At the beginning, final endocrine summaries were sent out to home medical institutions at places of permanent residence of study subject, but since June 2000 they were being dispatched personally to the home address of each study subject.

Implementation of the collaborative Ukraine-USA Thyroid Project was approved by the Ethical Committee of the National Cancer Institute (USA) and by the Ethical Commission of the Institute of Endocrinology and Metabolism (Ukraine). All potential study subjects (or the parents of those study subjects who had not reached the age of 16 years at the time of first screening examination) gave a written Informed consent to participation in medical screening examinations in the framework of the Project.

Screening examination forms of Project study subjects

There are two types of forms used for the study: management forms to document and support administrative aspects of the Project, and data collection forms to record information collected from each of the study subjects.

During medical examination of study subjects, medical team staff fill in the following forms: "Informed Consent Form"; "Control Form"; "Primary Registration Form"; "Locator Form"; "Initial Interview Form"; "Ultrasound Examination Form"; "Thyroid Palpation Form"; "Individual Medical Questioning Data (Medical Anamnesis Form)"; "Preliminary Conclusion and Medical Screening Recommendations Form"; "Blood Collection and Processing Form"; "Blood Laboratory Examination Results"; "Urine Collection, Processing, and Examination Form"; "Registration Log"; "Final Endocrine Summary and Recommendations Form"; "Fine Needle Aspiration Procedure Form"; "Cytology Conclusion Form"; "Hospitalization Form"; "Pathology Form"; "Nonresponse Form"; and "Death Data Form".

At the first stage of cohort selection before subjects' identification has started, all records on subjects were sorted out at random, after which each of the potential study subjects were assigned consecutively a unique identification number so as to exclude any possibility of determining the thyroid exposure dose for a subject according to his/her number. A subject's identification number consists of eight digits: the first six ones represent a unique individual number, and the last two is a reference number – the sum of the first six digits. The initially determined identification number is used for identification of a potential study subject according to any data related to this subject. This number may not be changed, excluded, or assigned to any another potential study subject, which warrants the linkage between a subject and his/her data and excludes the possibility of data loss or assigning them to another subject.

Most screening forms are coded, entered into a computer, and undergo quality

control, after which paper forms are stored in central archives, and computer files at the Data Coordinating Center, with a limited right to access.

After diagnosis has been established, the final endocrine summary is dispatched to each of the study subjects. The summary includes: study subject's surname, first name and patronymic; date of birth; identification number; home address; results of laboratory tests (thyrotropic hormone, antibodies to thyroid peroxidase, thyroglobulin, ionized calcium, antibodies to thyroglobulin, free thyroxine and parathyroid hormone); results of ultrasound examination of the thyroid; results of extra examination (fine-needle aspiration biopsy results, type of surgery, results of pathomorphology study); conclusion of the endocrinologist; recommendations.

The conclusion is recorded on an official form of the Project and signed by the endocrinologist. After conclusion, additional information is given, concerning the dates of the following regular medical examination, conditions of extra in-depth medical examination, as well as additional information: contact telephones of the screening Center and of the specialist responsible for in-depth medical examination.

Procedure of processing of study subjects' screening forms

Hard copies of primary Form sets, static and dynamic ultrasound thyroid images on electronic carriers, blood serum samples (in duplicates) for hormonal examinations and urine samples for iodine level determination, are obtained as a result of regular examination of study subjects. After completion of study subjects' examination, the fact of examination is recorded, expertise of primary endocrine conclusion is performed, and the whole set of primary Forms is registered in the Database of the Project. After processing of blood samples and registration of their findings, a complete set of Forms is made up, so that the endocrinologist who has directly performed study subject's medical examination can establish a final endocrine summary. If necessary, the endocrinologist refers the subject for extra examination (hormonal, ultrasound, cytological, etc.). After verification by the quality control officer, final endocrine summary with processed and registered urine samples is entered into the electronic Database of the Project, printed out and mailed to study subjects to their address of permanent residence.

Procedure of entering of information into electronic Forms includes double coding and double entry of data, elimination of discrepancies and 10% random control by the supervisor, verification of logical links, errors' registration, and introduction of necessary corrections. All electronic information in the Project Database is stored in two groups of files: "Original" (primary data obtained directly in the course of performance of an appropriate procedure) and "Edited" (residual data obtained after introducing the necessary corrections and additions into the primary data).

System of programme-informational support of the Project

The system of information-program support of the Project includes a set of key information components (a system for processing of screening data Forms, a unit of epidemiology information, a medical information system, and a dosimetry data component), program tools, and algorithms of information interaction between Project investigators. The unit of epidemiology information and medical information system, pooled in the central Database of the Project, are stored using MS SQL Server means, and for processing of screening Form data standard programs Access and SPSS are used. To ensure current activities of all Project areas, the program complex of user named IVA, developed with Delphi program, is used.

System of quality control of Project implementation

At all stages, permanent quality control of Project implementation is performed in order to collect high-quality data; with this purpose a group responsible for quality control has been established, a special manual of quality control has been developed, and appropriate procedures and methods of monitoring

documented. The Quality Control Group comprises the Head and specialists in quality control from all disciplinary areas of the Project: epidemiology, endocrinology, ultrasound investigation, cytology and pathomorphology study, laboratory examinations, dosimetry, data management and some other specialists. All Group's members have received a training by the specialists of the National Cancer Institute (USA) and obtained appropriate certificates. Quality control procedures are described in detail in the Manual of Operations and in a special Manual of Quality Control which includes forms-tables of reference tests for quality control of Project implementation and statistical report forms, as well as instructions for completion of these forms.

Direct observation – by quality control specialists – of appropriate procedures is performed both in regular and extraordinary regimes. So, in the fixed and mobile teams 100% of study subjects' lists and prepared questionnaires are checked; 2.5% of daily volume of work according to completed quality control forms, operator's positions of all team members (quarterly), questioning of study subjects on the quality of medical team operation, etc. Also, each quality control specialist checks 2.5% of screening forms – concerning his area of expertise for completeness and correctness of completion of the forms. The results obtained by the quality control specialists are reviewed at meetings of the Quality Control Group once every two months.

During preparation of this paper were used following data**:** place of residence of the study subjects and final endocrine conclusions are given as for the time of first screening medical examination; age of the study subjects – for the time of Chornobyl accident; individual doses of thyroid irradiation of the study subjects are presented according to direct measurements of the accumulation of radioactive iodine immediately after accident at the Chornobyl nuclear power station followed by calculation of the thyroid doses by specialists of Dosimetry Group (version of the first screening)

Study Results and their discussion

Examination of potential study subjects

As the lists of potential study subjects who have given their preliminary consent to participate in screening examination were assembled, staff of Project Epidemiology Group planned monthly trips of Project mobile teams to the selected controlled raions taking into account the proposals of local medical staff of these raions. 2-3 weeks before screening has started, invitation letters stating the place and time of examination were sent out to potential study subjects of the raion (100-150 persons on average, which was due to the work quota of medical team's staff). Appropriate lists of potential study subjects were also transmitted to local medical staff for personal contact with and additional invitation of subjects on the eve of the day of screening.

For the period April 1998 to December 2000, Project's mobile teams have been working every week in the local medical institutions (home hospital, polyclinic, outpatient clinic, or post of obstetrical aid) of controlled raions of Zhytomyr, Kyiv, and Chernihiv oblasts, except for Polisya, Prypyat, and Chornobyl raions of Kyiv oblast, which – according to a Governmental Decree – were included in the area of obligatory relocation of all inhabitants. Potential study subjects who were residing in Kozelets raion of Chernihiv oblast, were being screened by the fixed team at the Institute of Endocrinology and Metabolism in Kyiv, and their free transportation to the Institute and back was organized. Other potential study subjects who so desired or were living outside the controlled raions, could also have been screened by the fixed team. Several times, mobile teams were performing screening in other raions of Zhytomyr and Kyiv oblasts in areas with dense population of potential study subjects.

For the period April 1998 to December 2000, 13243 potential study subjects have undergone medical examinations (Table 1). More than a half of all screened persons (51.2%) were residents of Chernihiv oblast, 26.9% of Zhytomyr oblast, and 15.0% of Kyiv oblast. Among those screened, 56.9%

Table 1 – Characteristics of study subjects: examined

#	Administrative and territorial units	Total number of subjects	Distribution of study subjects								
			by dose, Gy			By age, years				by gender	
			<0.3	0.3-1.0	>1.0	≤4	5-9	10-14	≥15	females	male
1	Zhytomyr oblast	3562	1127	1211	1213	1208	1001	1113	240	1805	1757
1.1	Narodychi raion	864	100	265	498	276	242	259	87	447	417
1.2	Ovruch raion	2248	952	834	456	782	658	709	99	1103	1145
1.3	Other raions	450	75	112	259	150	101	145	54	255	195
2	Kyiv oblast	1989	1215	516	258	434	594	752	209	1040	949
2.1	Ivankiv raion	795	598	161	36	161	227	320	87	395	400
2.2	Other raions	1194	617	355	222	273	367	432	122	645	549
3	Chernihiv oblast	6785	4753	1453	570	2627	2044	1815	299	3409	3376
3.1	Kozelets raion	1833	1457	320	50	786	481	453	113	940	893
3.2	Ripky raion	1503	1124	293	85	519	473	455	56	764	739
3.3	Chernihiv raion	1918	1047	522	347	737	581	516	84	877	1041
3.4	Chernihiv city	1492	1104	304	84	571	497	383	41	809	683
3.5	Other raions	39	21	14	4	14	12	8	5	19	20
4	Kiev sity	877	431	283	163	251	286	273	67	460	417
5	Other oblasts	25	9	5	11	7	10	5	3	12	13
6	Other countries	5	5	0	0	1	0	3	1	3	2
7	Total	13243	7540	3468	2215	4528	3935	3961	819	6729	6514

of persons had a thyroid exposure dose under 0.3 Gy; 26.2% between 0.3 and 1.0 Gy; and 16.7% a dose over 1 Gy (information was missing for 20 persons). At the time of the Chornobyl accident, 34.2% of persons were aged up to 4 years; 29.7% were 5 to 9 years old; 29.9% from 10 to 14 years; 6.2% were aged 15 to 18 years. Among those screened 50.8% were females and 49.2% males.

9441 potential study subjects (71.3% of the total number of those screened) have been screened by mobiles teams at places of permanent residence or provisional stay, and 3802 potential study subjects (28.7%) have been examined by the fixed team at the Institute of Endocrinology and Metabolism. In particular, 1622 residents of Kozelets raion of Chernihiv oblast (42.7% of the total number of subjects screened by the fixed team), 858 residents of the City of Kyiv (22.6%), 825 residents of uncontrolled raions of Kyiv oblast (21.7%), and 350 residents of uncontrolled raions of Zhytomyr oblast (9.2%) have had screening by the fixed team.

Unfortunately, for a certain part of study subjects data were found to be missing about their participation in one or even several screening stages, in particular, blood examination (for 8 study subjects, or 0.1% of the total number of those screened), ultrasound examination of the thyroid (for 135 study subjects, or 1.0%), examination by the endocrinologist (for 13 study subjects, or 0.1%), urine examination (for 62 study subjects, or 0.5%), and dosimetry interview (for 1116 study subjects, or 8.4%) (Table 2). The main reason for absence of data was refusal of study subjects to undergo an appropriate screening stage; however, in some cases it was unsuccessful examination performance or sample collection, loss of sample or Primary Form, etc. In case of missing data on registration or endocrinologist's examination, potential study subjects were included in the list of those who had not had screening examination on a scheduled day, and these subjects were further invited again to screening by sending another invitation, by telephone conversation, or by involving local medical staff (at subject's place of residence) in invitation procedure.

Characteristic of study subjects in the first screening

At the moment of first screening examination, 7244 study subjects (54.7% of the total number of those screened) were permanent residents of rural type settlements (villages and properly settlements), and 5999 study subjects (45.3%) resided in urban type settlements and

Table 2 – Completeness of examination of potential study subjects

#	Administrative and territorial units	Total number of subjects	Stations of medical screening					
			registration	blood collection	ultrasound examination of the thyroid	examination by the endocrino-logist	urine exami-nation	dosimetry questioning
1	Zhytomyr oblast	3562	3562	3559	3510	3558	3546	3350
1.1	Narodychi raion	864	864	864	839	863	861	787
1.2	Ovruch raion	2248	2248	2245	2223	2245	2236	2141
1.3	Other raions	450	450	450	448	450	449	422
2	Kyiv oblast	1989	1989	1987	1979	1987	1977	1723
2.1	Ivankiv raion	795	795	794	787	794	787	683
2.2	Other raions	1194	1194	1193	1192	1193	1190	1040
3	Chernihiv oblast	6785	6785	6782	6719	6779	6752	6211
3.1	Kozelets raion	1833	1833	1833	1826	1833	1824	1618
3.2	Ripky raion	1503	1503	1501	1493	1499	1489	1393
3.3	Chernihiv raion	1918	1918	1918	1882	1918	1911	1764
3.4	Chernihiv city	1492	1492	1491	1480	1490	1489	1400
3.5	Other raions	39	39	39	38	39	39	36
4	Kiev sity	877	877	877	870	876	876	817
5	Other oblasts	25	25	25	25	25	25	21
6	Other countries	5	5	5	5	5	5	5
7	Total	13243	13243	13235	13108	13230	13181	12127

towns. 2110 study subjects (15.9%) resided in raion administrative centers, 1544 study subjects (11.6%) in oblast administrative centers, and 877 (6.6%) in the City of Kyiv.

The social status of study subjects was as follows: schoolchildren or students (4309 persons or 32.5%), industrial workers (1719 persons or 13.0%), specialist (1272 persons or 9.6%), agricultural workers (576 persons or 4.3%), manager (281 persons or 2.1%), others categories (1511 persons or 11.4%) and 3575 persons (27.1%) had no permanent work.

The marital status of study subjects was as follows: 8391 study subjects (63.4%) were unmarried, 4636 study subjects (35.0%) were married, and information was missing for 216 study subjects (1.6%). 7306 study subjects (55.2%) had a one brother or sister, 2913 study subjects (22.0%) had a two siblings, 1599 study subjects (12.1%) had three or more ones. 1080 study subjects (8.1%) had neither brothers nor sisters, and information was missing for 345 study subjects (2.6%).

Additional examination of study subjects

In connection with abnormalities in thyroid system status of study subjects (based on the data of ultrasound examination or examination by the endocrinologist) that had been detected during the first screening, it was found to be necessary to conduct a deepened extra examination (in particular, additional blood examination, additional ultrasound examination of the thyroid, fine-needle aspiration biopsy of the thyroid), or a course of treatment at the Clinic of the Institute of Endocrinology and Metabolism.

Blood examination was performed to 267 study subjects (2.0% of the total number of those screened), ultrasound examination of the thyroid was performed to 234 study subjects (1.8%), fine-needle aspiration biopsy of the thyroid was performed to 287 study subjects (2.2%), including 69 study subjects where biopsy was performed two times or more for objective reasons (Table 3). 83 study subjects (0.6% of the total number of those screened) were hospitalized at the Clinic of the Institute of Endocrinology and Metabolism for medical treatment and were operated on.

Preparation of final endocrine summary

Based on the results of ultrasound examination of the thyroid, blood examination (thyrotropin stimulating hormone, free

Table 3 – In-depth examination of study subjects

#	Administrative and territorial units	Screening stages												
		blood examination				ultrasound examination of the thyroid				fine-needle aspiration biopsy of the thyroid				thyroid surgery
		total	1	2	≥3	total	1	2	≥3	total	1	2	≥3	total
1	Zhytomyr oblast	78	75	3	0	75	71	3	1	75	61	13	1	25
1.1	Narodychi raion	35	34	1	0	33	31	1	1	25	21	4	0	11
1.2	Ovruch raion	38	36	2	0	36	35	1	0	33	25	7	1	7
1.3	Other raions	5	5	0	0	6	5	1	0	17	15	2	0	7
2	Kyiv oblast	32	28	2	2	33	28	3	2	44	33	8	3	11
2.1	Ivankiv raion	22	18	2	2	23	19	2	2	16	11	4	1	4
2.2	Other raions	10	10	0	0	10	9	1	0	28	22	4	2	7
3	Chernihiv oblast	131	110	14	7	104	93	9	2	147	108	28	11	40
3.1	Kozelets raion	62	57	5	0	46	46	0	0	31	22	6	3	7
3.2	Ripky raion	15	15	0	0	10	10	0	0	28	19	8	1	3
3.3	Chernihiv raion	25	15	5	5	26	21	4	1	56	38	12	6	21
3.4	Chernihiv city	29	23	4	2	46	46	0	0	31	28	2	1	8
3.5	Other raions	0	0	0	0	0	0	0	0	1	1	0	0	1
4	Kiev sity	26	22	3	1	22	18	3	1	20	16	2	2	7
5	Other oblasts	0	0	0	0	0	0	0	0	1	0	1	0	0
6	Other countries	0	0	0	0	0	0	0	0	0	0	0	0	0
7	Total	267	235	22	10	234	210	18	6	287	218	52	17	83

thyroxin, antibodies, thyroglobulin, and ionized calcium levels) and personal examination, the endocrinologists have completed 13214 final endocrine summaries nearly for all study subjects having had first screening examination (Table 4). Unfortunately, for 29 study subjects (0.2% of the total number of those screened) the summaries have not been completed as yet, for objective reasons: most of these study subjects need – for the clinical diagnosis to be established – a deepened extra examination (first of all, fine-needle aspiration biopsy of the thyroid), at the Clinic of the Institute of Endocrinology and Metabolism; however, for different reasons these subjects refuse to.

The terms of sending final endocrine summaries to the home medical institutions at places of permanent residence or directly to the home address of each study subject, were as follows: up to 3 months – 9.5%; 4-6 months – 42.3%; 7-9 months – 27.6%; 10-12 months – 11.0%; 13-18 months – 5.1%; 19-24 months –

Table 4 – Timeline of preparation of final endocrine summary

#	Administrative and territorial units	Total number of subjects	Total number of summary	Terms of dispatching, months						
				≤3	4-6	7-9	10-12	13-18	19-24	>24
1	Zhytomyr oblast	3562	3553	362	1599	1130	193	137	43	89
1.1	Narodychi raion	864	860	117	207	364	86	30	22	34
1.2	Ovruch raion	2248	2244	222	1095	672	87	100	19	49
1.3	Other raions	450	449	23	297	94	20	7	2	6
2	Kyiv oblast	1989	1985	244	1035	373	199	101	7	26
2.1	Ivankiv raion	795	794	51	209	309	150	53	1	21
2.2	Other raions	1194	1191	193	826	64	49	48	6	5
3	Chernihiv oblast	6785	6773	455	2649	1977	936	390	219	147
3.1	Kozelets raion	1833	1833	207	548	590	202	136	95	55
3.2	Ripky raion	1503	1499	81	644	237	360	86	54	37
3.3	Chernihiv raion	1918	1913	71	918	543	185	101	48	47
3.4	Chernihiv city	1492	1489	89	523	597	185	65	22	8
3.5	Other raions	39	39	7	16	10	4	2	0	0
4	Kiev sity	877	873	190	291	165	113	50	49	15
5	Other oblasts	25	25	1	14	5	3	0	1	1
6	Other countries	5	5	0	0	1	3	0	0	1
7	Total	13243	13214	1252	5588	3651	1447	678	319	279

2.4%; more than 24 months – 2.1% of the total number of summaries sended.

The main reasons for a longer term of final endocrine summary preparation at the initial stage of Project implementation were as follows: the necessity to develop, introduce, and test the system and software for computer processing of the results of examination of study subjects and summary preparation; certain difficulties with delivery of kits for determination of hormonal and antibody levels; insufficient staff of collaborators for laboratory examination performance and computer processing of the results of examination of study subjects; insufficient technical support of the procedures of laboratory examinations; and computer processing of the results of examination of study subjects.

Besides, the duration of final endocrine summary preparation was determined by the necessity for an in-depth examination to a part of the study subjects: in particular, performance of fine-needle aspiration biopsy of the thyroid in case of nodular pathology, part of the results of which were found to be poorly informative or non-informative, which required performance of a repeat manipulation in a certain time interval, thus delaying conclusion preparation. Moreover, the necessity for testing parathyroid hormone level in the presence of a deviation in the indices of ionized calcium owing to an extremely low hypocalcemia among study subjects, also determined longer time intervals between investigations using radioimmunological or immunoenzymic kits, delaying final endocrine summary preparation.

Unfortunately, part of study subjects did not attend in time for in-depth examination (in particular, thyroid biopsy, extra hormonal examination, etc.) for the same subjective and objective reasons which were typical of study subjects' non-attendance for regular medical examination (in particular, uninterested in his/her health status; fear of medical manipulations, financial problems or lack of time to come to the Institute; disease; business trip, studies, military service, and other).

However, in the course of Project implementation a gradual decrease was noted both in average duration of final endocrine summary preparation and in the percentage of these conclusions with a long term of dispatching final endocrine summaries to local medical institutions at subject's permanent place of residence, or directly to the home address of each of the study subjects.

Conclusion

Implementation of the joint scientific Ukraine-USA Thyroid Project allowed to involve in a complex examination of thyroid status a 13243 residents of the most contaminated, as a result of the Chornobyl accident, areas of Zhytomyr, Kyiv, and Chernihiv oblasts, and to obtain scientific data on the relationship between thyroid diseases (first of all, malignant tumors) and the level of exposure to iodine-131.

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