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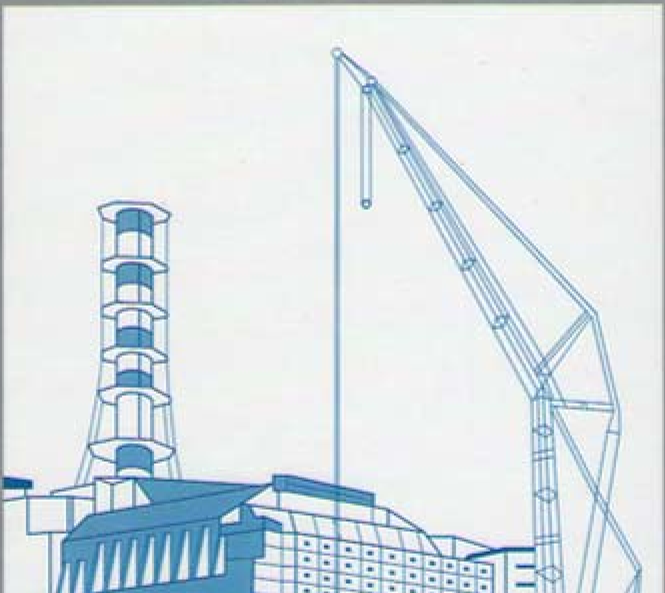
International Congress Series 1234

Chernobyl: Message for the 21st Century



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and Kingo Fujimura

Chernobyl: Message for the 21st Century

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Proceedings of the Sixth Chernobyl Sasakawa Medical Cooperation Symposium,
Moscow, Russia, 30–31 May 2001

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2002

ELSEVIER

Amsterdam – London – New York – Oxford – Paris – Shannon – Singapore – Tokyo

ELSEVIER SCIENCE B.V.
Sara Burgerhartstraat 25
P.O. Box 211, 1000 AE Amsterdam, The Netherlands

First edition 2002

Library of Congress Cataloging-in-Publication Data
Chernobyl Sasakawa Medical Cooperation Symposium (6th : 2001 : Moscow, Russia)
Chernobyl : message for the 21st century : proceedings of the sixth Chernobyl Sasakawa Medical Cooperation Symposium, held in Moscow, Russia 30-31, 2001/ editors, Shunichi Yamashita ... [et al.].-- 1st ed.
p. cm. -- (International congress series, ISSN 0531-5131 ; no.1234)
Includes bibliographical references and index.
ISBN 0-444-50869-4 (alk. paper)
1. Thyroid gland--Tumors--Congresses. 2. Chernobyl Nuclear Accident, Chornobyl§' Ukraine, 1986--Health aspects--Congresses. 3. Tumors, Radiation-induced--Congresses. I.Yamashita, Shun'ichi, 1952- II. Title. III. Series.

RC280.T6 C447 2001
616.99'444--dc21

2002021653

British Library Cataloguing in Publication Data
Chernobyl Sasakawa Medical Cooperation Symposium (6th : 2001 : Moscow, Russia)
Chernobyl : message for the 21st century : proceedings of the Sixth Chernobyl Sasakawa Medical Cooperation Symposium held in Moscow, Russia, 30-31 May 2001. -
(International congress series ; 1234)
1. Chernobyl Nuclear Accident, Chornobyl', Ukraine, 1986 - Health aspects - Congresses
2. Radiation injuries in children - Ukraine - Chornobyl' - Congresses 3. Thyroid gland - Cancer - Ukraine - Epidemiology - Congresses 4. Thyroid gland - Radiation injuries - Ukraine - Epidemiology - Congresses 5. Medical assistance, Japanese - Ukraine - Congresses
I. Title II. Yamashita, Shunichi, 1952- 363.1'799' 094777

ISBN 0444508694

International Congress Series No. 1234
ISBN: 0-444-50869-4
ISSN: 0531-5131

∞ The paper used in this publication meets the requirements of ANSI/NISO Z39.48-1992 (Permanence of Paper).
Printed in The Netherlands.

Acknowledgements

The Nippon Foundation (http://www.nippon-foundation.or.jp) through Sasakawa Memorial Health Foundation provided financial support for the publication of this volume.

Preface

It is with deeply felt affection that we dedicate this book, *Chernobyl: Message for the 21st Century*, to the future of all of the children affected by the Chernobyl accident. This book contains the proceedings of the Sixth International Chernobyl Sasakawa Medical Cooperation Symposium, held in Moscow, Russian Federation on May 30–31, 2001. More than 180 participants attended the symposium, which was organized as a forum to report the results of the second stage of the Chernobyl Sasakawa Health and Medical Cooperation Project (1996–2001) as well as to mark the project's completion. The project ran for 10 years from 1991 to 2001.

It was with mixed feelings that we commenced this project—to help overcome the tragedy of Chernobyl, with the tragedies of Hiroshima and Nagasaki still on our shoulders. The first half of this project focused on the health screening of children in five areas affected by the Chernobyl accident, within Belarus, Russia and Ukraine, based on a common protocol and standardized procedures. The results were reported at the Fifth Chernobyl Sasakawa Medical Cooperation Symposium in Kiev in 1996, the proceedings being published as *Chernobyl: A Decade* by Elsevier Science as part of its International Congress Series. Thus this book serves as a follow-up to the first set of proceedings.

This book is composed of two parts: the first consists of addresses, presentations and a discussion of the Symposium, and the second invited papers by international experts written specifically for this volume.

Towards the end of the first (1991–1996) stage of the project, a dramatic increase in thyroid cancer among children, particularly living in the Gomel region of Belarus, came to our attention. To test the hypothesis that this increase was a result of the Chernobyl accident, we launched a study aimed at comparing the prevalence of thyroid diseases between children born before and after the accident in the Gomel region. We present the results in this volume.

We are very pleased to see, in the second stage of this project, formation of international communities around some of the health issues of the Chernobyl accident. These efforts include the international cooperation to establish post-Chernobyl NIS thyroid tissue, nucleic acid and data banks, as a collaborative project of Belarus, Russia, Ukraine, the EC, the National Cancer Institute of the USA and our Foundation, and the WHO Health Telematics project "Medical relief for children affected by the Chernobyl accident," conducted by Belarus, WHO and our Foundation. The scope of these activities is reported in the proceedings.

All through the ten years of the Chernobyl Sasakawa Health and Medical Cooperation Project, our basic stance has been that the project should be humanitarian *and* scientific. It was for the children who would build the future of humankind. It was for the children whose parents lived with the fear of uncertainty in the areas affected by the Chernobyl accident. The project centered around the health and welfare of those who had been child at the time of the accident, although the effects on the adult population were by no means ignored. We believed from the first that humanitarian acts of this kind must be based on solid scientific principles. Thus the data obtained from all screenings needed to be of high quality and bearable to the scrutiny of the world's scientific community, and could be shared by all when necessity arose.

It is our sincere wish that this volume of proceedings serves to contribute to build a more humane and peaceful world.

Kenzo Kiikuni
Chairman
Sasakawa Memorial Health Foundation

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Addresses

Ministry of Health of the Russian Federation

Gennadiy G. Onischenko, Deputy Minister

Japan was one of the first countries to react to the appeal for help made by WHO and the government of the USSR following the Chernobyl accident. International assistance was considerable. The financial support made through the government of Japan, which amounted to about 20 million US dollars, realized an international WHO program for minimizing the aftermath of the Chernobyl accident during the period from 1991 to 1994. Russian and Japanese scientists are continuing an active collaboration in research on radionuclide content in the environment of territories polluted by the Chernobyl accident.

Since 1995, the project for research on causes of thyroid diseases induced by the Chernobyl accident has been implemented jointly by Sasakawa Memorial Health Foundation and the International Agency for Research of Cancer in Lyon. Modern equipment for this project was purchased by Sasakawa Memorial Health Foundation, at a total cost of about 900 000 US dollars. The main aim of the research project was to clarify the involvement of radiation in the induction of thyroid cancer among children living in the most affected regions of the Russian Federation, i.e., Bryansk, Kaluga, Tula and Oryol regions. In the project, 500 children have already been examined and 72 cases of childhood thyroid cancer have been detected.

Another highly important medical project has been conducted since 1998 with the participation of Sasakawa Memorial Health Foundation, WHO, the Medical Radiological Research Center of the Russian Academy of Medical Sciences and the National Cancer Institute in the USA, as well as the Ministries of Health of Russia, Ukraine and Belarus. This project aimed at establishing a bank of thyroid tumor tissue, blood and blood components obtained from thyroid cancer patients who underwent surgical procedures. It is hoped that this project will allow us to make an objective estimation of the late effects of radiation received by the population of the Russian Federation. About 480 cases of thyroid cancer have been confirmed in the framework of the project and a considerable amount of tissue samples has been collected. We will continue this project in Russia regardless of what further collaboration we may receive.

At the end of the last millennium, both the people of Japan and the former Soviet Union faced the catastrophic effects of radiation exposure. It was perhaps these common experiences that drew the attention of Sasakawa Memorial Health Foundation to the Chernobyl accident. We earnestly hope that this collaboration will long continue, and I consider this symposium a step towards that goal. Further cooperation, primarily with Sasakawa Memorial Health Foundation, in the following areas will be of significant importance to achieving our aims:

1. Continuation of bilateral projects to clarify the mechanism of pathogenesis of thyroid cancer in children and adolescents; further support of the medical organizations and donations of essential equipment in Klincy and Obninsk of the Russian Federation;
2. Use of electronic sources of individual medical dosimetry information in the framework of the above-mentioned bilateral project;
3. Use of telemedicine technology aimed at urgent consultation at diagnostic centers of patients residing in radio-contaminated areas;
4. Extension of training of young Russian specialists in clinical bases and scientific centers;
5. Sanitation of children in Russian territory and abroad; and
6. Working out of appropriate scientifically based medical recommendations.

On behalf of the Minister of Health of the Russian Federation, Yu. L. Shevchenko, and the Board of the Ministry of Health of the Russian Federation, I would like to wish this symposium an overwhelming success. The Ministry of Health recognizes that the great work of the scientists involved in the collaboration from Sasakawa Memorial Health Foundation will be once again noted in the symposium, and most importantly the tasks for the future will be determined. We would like to thank all persons involved in this work.

Ministry of Health of Belarus

Igor B. Zelenkevich, Minister

The accident that occurred in Chernobyl 15 years ago is considered the largest technological catastrophe of the past century. As a result of the accident, a territory of about 46 000 square kilometers, inhabited by more than 2 million people (about 20% of Belarus' population), was polluted by long-life radionuclides such as cesium, strontium and plutonium. During the initial period after the accident, almost the entire population of Belarus was affected by radiation caused by radionuclides of iodine.

Because of the size of the contaminated territories and the considerable number of people affected by radiation and non-radiation factors of the Chernobyl catastrophe, the government of Belarus, the Ministry of Health and many scientists were obliged to investigate a new approach, to organize a new system for estimation of the health condition of the affected people, and to develop early diagnostics, treatment and rehabilitation. Very large expenses to resettle the population away from the contaminated areas were also required. We will continue to deal with those problems in future.

Estimation of the health condition of the population was carried out by screening 1.67 million people, among whom 350 000 were children. The data were accumulated in the Russian state registry of people affected by the Chernobyl catastrophe. The results of analyis of this information are still being studied both inside our health care system and in the framework of international projects. The results will be used to improve the health care of all people affected by the catastrophe.

The Chernobyl accident has badly affected the health of a great part of the Belarussian population. The increase of thyroid diseases, especially that of thyroid cancer in children, which has been demontrated to be a direct consequence of the accident, is of especial concern. Understanding of the pathogenesis of malignant tumors is one of the main tasks of medical science, and is possible only under close international cooperation. Belarus is open for implementation of international scientific projects in the field of medical care for the population.

Public figures and scientists from many countries, including Japan, USA, Germany, France and Italy, together with specialists from Belarus, have been working on the problems caused by the Chernobyl accident in our country for more than 10 years. Among our overseas collaborators, the contribution of Sasakawa Memorial Health Foundation is of particular note. Humanitarian and scientific projects of Chernobyl-Sasakawa have been carried out since 1991. Aside from one-time humanitarian action, the projects of Sasakawa Memorial Health Foundation have enabled the long-term study of the influence of low-dose radiation on children's health.

The Joint Japan-Belarus Chernobyl-Sasakawa centers have been built in the cities of Mogilev and Gomel on the foundations of pre-existing medical organizations. Regular visits of the Japanese specialists, and expensive medical equipment, consumables and medicines were donated to these centers. Screening was carried out both in the centers and in mobile laboratories supplied on Japanese automobiles.

Besides donating equipment to our country, Sasakawa Memorial Health Foundation provided considerable assistance in the form of consultations and education of staff in various aspects of endocrinology, hematology and dosimetry. Education was provided during visits by Japanese specialists and by training courses at leading centers of Japan. We exchanged opinions and data during regularly held symposiums. As a result of this work, we have covered the distance from complete non-understanding to at least partial knowledge, because 10 years is quite a short time in the study of such a large problem. Thus for this reason, I would like to express the hope that this research will continue into the future and that our knowledge will become deeper and wider.

We express our gratitude to Sasakawa Memorial Health Foundation, the president of The Nippon Foundation, Mr. Yohei Sasakawa, to Prof. Kiikuni, Prof. Nagataki and Prof. Yamashita, and to many, many others who took part in the projects and who have helped us and are continuing to help us to overcome the problem. I would also like to congratulate all of the organizers for holding a conference devoted to the Foundation's activities, and I wish you good health, success and excellent results. Thank you for your attention.

Ministry of Health of Ukraine

Olga A. Bobyliova, First Deputy Minister

The accident at the Chernobyl Nuclear Power Plant led to radiation pollution in 77 districts of 12 regions of Ukraine. Now, more than 2.5 million people are included on our dispensary control list, 529 000 of whom are children. Follow-up of the health condition of the affected people over the last 15 years has witnessed degrading health conditions in every category, and that of children is outstanding. The disease rate increased firstly due to diseases of the nervous system, which were of no specific character and presented as a form of vegetovascular dystonia, and diseases of the urogential system, skin and subcutaneous fat. The number of children born with abnormalities and deformity increased 8 fold following the accident; 40% of these births occurred during the last 5 years.

A considerable increase of thyroid cancer among children in Ukraine has been observed since 1990. According to the Institute of Endocrinology and Metabolism, more than 1600 people who were children or adolescents at the time of the accident underwent surgical procedures for thyroid cancer in Ukraine between 1986 and 2000. The most considerable increase in the incidence of thyroid cancer occurred in people who were aged up to 4 years at the time of the accident. The disease rate in this group increased more than 3.1 fold. There is a network of special medical organizations, namely radiation centers and radiation defense dispensaries for the examination of affected people, devoted to medical help in Ukraine. The total number of specialized beds is more than 3000. A network of expert commissions to determine causal connections of disease and invalidity is spread over the country. Control and monitoring of the population mortality index has been carried out. We have managed to stabilize and decrease the mortality of children in all areas contaminated by the Chernobyl accident, by constant medical follow-up and improvement of methods of diagnosis and treatment.

Considerable help and improvement in assisting those affected by the Chernobyl accident reached Ukraine through the two diagnostic centers in Kiev and Korosten in Zhitomir region, which were set up in the framework of the Chernobyl-Sasakawa project. Modern medical equipment in these centers, provided by Sasakawa Memorial Health Foundation, proved to be the most effective implements of all in solving our problems. Toyota laboratory buses, in which screening activities can be carried out, were donated to Ukraine. Ukrainian specialists in these centers received education and training from the best organizations in Japan in the fields of radiology, endocrinology and hematology. We are very grateful to the highly qualified Japanese specialists who, together with Ukrainian doctors, worked during all these years for the improvement of medical care for the affected people. We would like to express our gratitude in particular to Prof. Yamashita, Prof. Fujimura, Prof. Shibata and Prof. Hoshi, and to all of the others whom we so often saw in our country, and whom our people, our patients at the polluted territories, know and think of as their own doctors.

A total of 64 000 children were examined at the two Sasakawa-supported centers in Ukraine when the project was implemented. Autoimmune thyroiditis was found among those examined. There were up to 12 000 different pathology cases, and Ukrainian and Japanese specialists together tried to find out the reasons for their appearance.

Another important aspect of the implemented research, in our opinion, is that it was very much future-oriented. The program was significant in that it aimed at analyzing children's health and that it led to recommendations for the improvement of children's health and for managing risk factors. The underlying principle of the collaboration was to determine what should be done today and what should be done tomorrow. For this reason, priority was focused on children. The Japanese specialists made several visits to the Ukraine during the Chernobyl-Sasakawa project, and these helped reduce the biggest after-effects of the Chernobyl catastrophe: psycho-emotional tension among the affected population. Japanese specialists who are working and, we hope, will continue to work with Ukrainian specialists have gained enormous trust from their Ukrainian patients. The Ministry of Health remains very grateful to Sasakawa Memorial Health Foundation, to Mr. Sasakawa and to the specialists who worked in Ukraine all these years.

On behalf of the Ministry of Health, once more I would like to express our gratitude to Mr. Sasakawa, Sasakawa Memorial Health Foundation, all the specialists, and all our colleagues in Russia and Belarus who strengthened the project by their knowledge. We would like to wish this symposium a fruitful one for the welfare of all people affected by the Chernobyl accident, and to express hope for the continuation of projects such as the epidemiological survey of thyroid abnormalities, genetic monitoring, the unique bank for thyroid cancer tissue supported by Sasakawa Memorial Health Foundation, WHO and others, and the development of medical telecommunication. Let me express hope, and confidence, that we will find ways of collaboration and that the collaboration will develop further advances in science. I would also like to say that the Ukrainian government awards the special gratitude of the Prime Minister of Ukraine to the leading Japanese specialists who worked at the contaminated territories. Thank you.

EMERCOM of Russia

Nadezhda V. Gerasimova, Deputy Minister

Fifteen years have passed since what was the greatest technological catastrophe of the 20th century. The government of the Russian Federation has been trying to solve the consequences of it ever since. I would like to take this opportunity to say what the state has been doing to minimize the consequences of the Chernobyl catastrophe. The law "About social protection of citizens, affected by radiation as a result of the Chernobyl accident" was adopted in 1992. After the adoption of this law, three programs, "Chernobyl children" "Program for population's protection of Chernobyl consequences" and "Housing problem for the liquidators" in relation to Chernobyl were also adopted and are in effect now. Since the time the programs were adopted, considerable funds have been allocated to stabilize the economic situation of the radiation-contaminated territories. Initially, 14 regions of our country were polluted or had radioactive influence. Now, after 15 years of undertaking significant measures, we consider 4 regions, Kaluga, Tula, Oryol and Bryansk, contaminated. A considerable amount of work has been conducted in the agricultural sector to clear radionuclides and recover land.

All of the programs are to be finished in 2001, as planned. This is the reason for which, on the instruction of the government, the EMERCOM (Ministry of the Russian Federation for Civil Defense, Emergencies, and Elimination of Consequences of Natural Disasters) and other federal ministries and agencies intend to carry out programs for liquidation till 2010 of the consequences of the Chernobyl accident, nuclear weapon tests in Semipalatinsk, and the accident at "Mayak" manufacturing enterprise. Now the programs are almost ready and have been adjusted with other ministries and agencies. Experts have examined the programs, and they will be reviewed at a session of the Government of the Russian Federation in June. The program is to build all of the objectives, mostly of health care that were started before, and the rest should be oriented for practical measures and scientific work.

However, it must be emphasized that, with regard to the Chernobyl tragedy, the consequences of liquidation will continue even after the programs end in 2010, and that environment monitoring should be conducted for a long time after that date. Many problems connected with forestry in the contaminated territories, and equally many problems connected with monitoring the health of the population, remain unsolved. A medical registry, in which more than 500 000 of the liquidators and people affected by radiation are listed, has been created here. Similar registries exist in Belarus and the Ukraine.

The Government of the Russian Federation has taken considerable measures to provide assistance to liquidators of consequences of the accident at the Chernobyl Nuclear Power Plant. There are, we believe, more than 200 000 liquidators in the Russian Federation. The Government of the Russian Federation has instructed the exchange of certificates of those who participated in liquidating the consequences of the accident at the Chernobyl Nuclear Power Plant this year and the following. Currently, the certificates in use are those of the Soviet Union. We have faced several problems, especially in Caucuses republics, where certificates are forged. The certificates of those who participated in liquidation will be exchanged to provide possible assistance only to those who require it. A program to provide the liquidators with dwellings has not yet been completed. Only 30% of liquidators who were involved in the program have received dwellings. There are more than 11 000 square kilometers of dwellings. In total, 9000 families have received dwellings and about 30 000 are in need of improvements of their own dwelling. A new law concerning compensation for damage to health, primarily on the liquidators, was adopted this year, as the liquidators had previously received a very small assistance to compensate for health effects. About 99.3% of the population are satisfied with the law, because the invalids of the 1st category (about 60%) had been receiving up to 500 rubles per month, and now they will receive 5000 rubles per month; invalids of the 2nd category 2500 rubles per month and those of the 3rd category, about 1250 rubles per month. This represents only compensation for harm to health and does not include other payments and social privileges, of which the Russian Federation provides about 30 different categories. This is undoubtedly only a very small amount of what the state can do for the people whose health was affected, but contributes to the liquidation of the largest accident of the 20th century.

We will continue to work on improving the laws for the social protection of citizens. A new law, the "dose law," has been discussed at a government session. According to this law, from 2003, privileges and compensations are planned for those who are exposed to radiation exceeding 1 mSv per year over the technological level existing in Russia. Another law was adopted in 1996, effective January 1, 2000, stating that if a person is exposed to radiation exceeding 1 mSv per year against natural background levels, the person should be provided with social privileges. Visiting different territories, and observing activities there, I must say that a lot of work has been done, and a good quantity of it has been carried out by international non-government organizations. At the same time, we have a huge amount of problems that we have failed to solve, especially concerning the long-term prospects of the health condition of the population. I would like to express true gratitude to Sasakawa Memorial Health Foundation, which was the first organization to offer a helping hand to the three affected countries—Ukraine, Belarus and

Russia. I would also like to extend our gratitude to Sasakawa Memorial Health Foundation on behalf of the people who received radiation exposure. I hope that this symposium will have a great beneficial effect for our people in the future. Only those who experienced the tragedy can estimate its consequences, and can understand and feel what help is necessary for the people who suffered the same tragedy in Japan.

Thank you very much. We hope for further collaboration with you, and we are thankful for the great assistance you gave us. I wish you good luck in the symposium.

The Nippon Foundation

Yohei Sasakawa, President

I am pleased to be here today at the opening of this International Sasakawa Chernobyl Symposium to greet you on behalf of The Nippon Foundation. This Symposium has been organized to commemorate the Tenth Anniversary of the Chernobyl Sasakawa Health and Medical Cooperation Project.

In early 1990, I visited Moscow as head of an economic mission. On that occasion, then-President Gorbachev asked me if there was anything I could do to aid the victims of the Chernobyl accident. My country is the only country to have experienced the terrors of an atomic bombing. Thus, it was my strong conviction that there was no country better suited than Japan to provide assistance.

On return to my country, I immediately consulted with Dr. Itsuzo Shigematsu, one of the foremost experts on radiation medicine in Japan. He agreed with me that we should gather a team of experts from Nagasaki and Hiroshima to study how to help. A group of the best qualified people in the world was thus brought together.

Building on the experiences of Nagasaki and Hiroshima, our group decided to do two things. First, we would try to ease the fears of the people in the Chernobyl area. Second, we decided to conduct extensive medical examinations of its children.

I was determined that I would make this project humanitarian aid in the true sense of the word. This must be the aid , not only for the people of a region, but for all of humanity. Thus, we decided that the project had to have a firm scientific basis. Then, when President Gorbachev came to Japan in April of 1991, he allowed us to use the Antonov — the world's largest military transport plane. Using this giant aircraft, we sent five mobile examination vehicles, the most-up-to-date equipment for treatment, supplies and medicine, to Moscow. There, on the anniversary of the Chernobyl Accident, we initiated the whole program in Red Square.

Over the next five years from 1991 to 1996, we examined about 160 000 children in five locations in Russia, Belarus and Ukraine. According to my original plan, the project was to end here. However, we had discovered an enormously high prevalence of thyroid cancer in the Gomel region of Belarus. Thus, I extended the program for another five years, focusing on this area.

Over the ten years to date, we have provided about 50 million US dollars in funding to support this program. In the end, the number of children screened totaled over 200 000. We have donated fifteen mobile examination vehicles. They have traveled a distance equal to roughly ninety times the length of the equator. In addition, about six hundred medical personnel have traveled back and forth between the Chernobyl region and Japan.

The volume of equipment, medicine and supplies was also impressive. This was a truly large project. The result of our steady screening program is a massive collection of data. Should a similar accident occur again in the future, and I hope it doesn't, this data will be of immeasurable value.

But I firmly believe that this difficult program would not have succeeded on grant money alone. It was all of us, working so hard together, that brought it such success. The cooperation and understanding of the governments of Russia, Ukraine and Belarus were vital. Then, Aeroflot provided aid more than forty times by transporting supplies and personnel at very low prices. Above all, it was the devotion of individual people that made this project possible: the selfless medical staff in the region who cared for the health of the residents, and dedicated specialists from Japan. They played absolutely vital roles. To all of these people and groups, I extend my deepest gratitude.

Over the past ten years, many international aid organizations and NGOs have contributed to the rescue of the region. However, very few of them persisted for that entire period. I am very proud that The Nippon Foundation and Sasakawa Memorial Health Foundation are in the small group that did. For us, the key words that helped us to sustain our effort were "patience" and "continuity."

I firmly believe that the trusting relationship built among all the people who worked for this project and the things learned together will never fade away. These strong bonds, the peace of mind of the residents of the region and the network of people and technology will only continue to grow stronger in the future. This is not simply a "thing" that I have given to the people of Chernobyl. Rather, you could say we have helped raise the children of the region. Let us all look forward together to their bright future.

I thank you all for your help over the past ten years.

World Health Organization

Michael Repacholi, Coordinator, Occupational and Environmental Health

On behalf of the World Health Organization (WHO), I am pleased to add my sincere thanks to you for coming to Moscow and welcome to this important symposium of the International Chernobyl Sasakawa Project.

WHO was associated from the very beginning with many of the activities related to the Chernobyl accident. Just over 7 days following the announcement of the accident, WHO convened a meeting at its Copenhagen office to evaluate the consequences and to make preparations for the catastrophe that followed. With the contribution of some 20 million US dollars from the Government of Japan and a number of other countries, WHO was able to begin a large humanitarian effort to build up the health care systems in the 3 affected countries of Belarus, Russia and Ukraine, and to conduct studies of victims of the accident.

During this period, WHO has been pleased to be associated with the excellent works of the Sasakawa Memorial Health Foundation. Our activities continue to this day...15 years after the accident. Collaboration with Sasakawa has been both meaningful and very beneficial to the affected populations and WHO has been pleased to be associated with these activities.

Let me add my thanks to the organizing committee, and particularly Sasakawa Memorial Health Foundation for inviting WHO to the prestigious symposium. On behalf of WHO I wish you all an enjoyable stay in Moscow and that the symposium will be both scientifically stimulating and worthwhile.

Thank you.

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Chernobyl Sasakawa Health and Medical Cooperation Project

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Sasakawa Chernobyl Scientific Committee, 4-8-8 Yakumo, Meguro, Tokyo, 152-0023 Japan

Abstract

The Chernobyl Sasakawa Health and Medical Cooperation Project was launched in May 1991 and its 5-year programs were completed in April 1996. Measurements of exposed radiation dose, thyroid examinations and blood tests were conducted for children in the five regions of the Ukraine, Belarus, and Russian Federation contaminated by radioactive substances from the Chernobyl accident. Examination of about 160 000 children revealed that thyroid nodules and thyroid cancers were prevalent in Gomel, the most heavily contaminated among the five regions. However, no increases in leukemia were observed in any of the five regions. An additional 5-year project was initiated in May 1996 and completed in April 2001. The project programs included a case-control study on childhood thyroid cancer, a follow-up thyroid examination of children exposed to radiation and a health examination of children born after the accident. A telemedicine program between the Gomel Center and Nagasaki University School of Medicine, and an international cooperative project to establish thyroid cancer tissue banks are also being implemented. It is expected that all these programs have contributed to their original objectives, which were to provide support for the three Republics in their efforts to supply the best medical care for the people affected by the Chernobyl accident. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Chernobyl accident; Sasakawa Project; Thyroid cancer; Tissue bank; Telemedicine

The Chernobyl Sasakawa Health and Medical Cooperation Project was launched in May 1991 in response to the request from the former Soviet government. Furthermore, its 5-year programs were completed in April 1996. An additional 5-year project was initiated in May 1996 and completed in April 2001. This paper intends to summarize the total 10-year Chernobyl-related activities of Sasakawa Memorial Health Foundation (SMHF).

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PII: S0531-5131(01)00589-1

When the Chernobyl nuclear power plant accident occurred in April 1986, international aid was extended by various organizations. These include international organizations such as the United Nations (UN), the World Health Organization (WHO), the International Atomic Energy Agency (IAEA) and the European Union (EU) as well as governmental agencies and nongovernmental organizations from many countries. However, for several years after the accident, such aid was mainly focused on investigations of the effects due to the accident and almost no aid was delivered directly to the residents in the affected areas.

Under these circumstances, the former Soviet government requested, in February 1990, assistance for the afflicted residents of Chernobyl from SMHF, which has a notable record of achievement in international medical cooperation. Upon receipt of the request, the "Chernobyl Sasakawa Health and Medical Cooperation Project" was created with the collaboration of the Japan Shipbuilding Industry Foundation (now the Nippon Foundation). A mission to survey how to best implement the project was dispatched in August 1990. The mission's report highlighted the following five points:

1. Fear and anxiety were so pervasive among residents in the affected areas.
2. One of the reasons for such fear and anxiety was lack of accurate information.
3. It was imperative to identify health problems among the residents.
4. Direct health examinations were considered to be the most suitable response to this problem.
5. Children who were most sensitive to radiation should be given priority.

Based on this report, the five regions, namely, Kiev and Zhitomir in the Ukraine, Gomel and Mogilev in Belarus and Bryansk in the Russian Federation were selected from the areas contaminated by radioactive substances from the accident. It was also decided to implement a 5-year health examination program targeted at the children at the time of the accident in these five regions. In May 1991, the examinations began with one Health Examination Center established in each of the five regions. Three major items, measurements of exposed radiation dose, thyroid examinations, and blood tests were covered by the examinations. During the 5-year period completed in 1996, altogether about 160 000 children were examined at the five centers.

The main items implemented by the 5-year programs are summarized in the following seven points. Total expenditure of the project reached more than US$30 000 000.

1. Donation of five mobile units for health examination equipped with whole body counters, supersonic thyroid diagnostic machines, blood analysis equipment and 10 passenger buses for transportation of children.
2. Provision of a complete set of the above equipment to each of the five centers.
3. Supply of various medical equipment, supplies, pharmaceuticals and personal computers.
4. Dispatch of experts from Japan to the area (about 90 times, total of 310 persons).
5. Technical training in Japan and on-site for the center's staff in charge of the examinations (13 times, total of 130 persons).
6. Educational activities for residents in the affected areas.

7. Presentation of the results of the examinations (four lectures for the residents, six workshops and five symposia).

According to the proceedings of the symposia and workshops mentioned in item 7 above [1–5], the actual status of internal cesium 137 dose was made clear to some extent and no serious exposure was observed at the time of examination, but it was reported that to identify the exposed radiation dose immediately after the accident is important. The thyroid examination revealed a variety of thyroid abnormalities. The detection rates of thyroid nodule and thyroid cancer were highest in the Gomel region in Belarus, the most heavily contaminated with radioactive substances among the five regions. It was thus pointed out that further study on the relation with radiation exposure and with an iodine shortage is necessary. Furthermore, since blood tests did not reveal any increase of leukemia that had been anticipated, it was indicated that follow-up blood examination should be continued.

As mentioned earlier, the first 5-year programs were finished in April 1996. However, reagents and other medical supplies and repairs of the equipment have been provided from time to time to support the autonomous health examination activities of the five centers. Also, an additional project was begun after May 1996 at the Gomel and Mogilev Centers in Belarus and at the Bryansk Center in the Russian Federation. It includes a case-control study on childhood thyroid cancer, a follow-up thyroid examination of children exposed to radiation and a health examination of children born after the accident. These additional programs have been carried out up to the present in cooperation with the International Agency for Research on Cancer (IARC) and the Medical Radiological Research Center (MRRC) at Obninsk. The results of these activities will be presented at this symposium.

Recently, using funds from the European Commission (EC), WHO, the National Cancer Institute (NCI) of the US and SMHF, three tissue registration banks were established at Minsk, Obninsk and Kiev for the purpose of preventing the dissipation and loss of the sample tissues from thyroid cancer operations and for ensuring management of the related data. At these tissue banks, international joint studies are being conducted in the areas of pathological and molecular biological research into thyroid cancer. Furthermore, since February 1999, Gomel Center—which has the highest incidence of thyroid cancer—and Nagasaki University School of Medicine in Japan have jointly used satellite communications to operate a remote medical care and diagnostic support system. At present, they perform thyroid diagnostic imaging using two sets of ultrasonic diagnostic equipment. Based on this means of telemedicine, WHO, in cooperation with SMHF, is promoting what is called the Health Telematics Project for the support of remote diagnoses and medical education in Belarus. A presentation concerning these new activities is also included in the agenda of the current symposium.

The effort of the Chernobyl Sasakawa Health and Medical Project has been focused on the humanitarian aid of providing health examinations to as many children in the affected areas as possible. To date, most children have had only one opportunity to undergo a health examination. However, it was felt necessary to provide additional support to maintain a continuing examination and follow-up care system for those examined and diagnosed with thyroid or blood abnormalities. I would like to emphasize that these procedures are now being activated at least as far as the five centers are concerned.

Begun in May 1991, this project has completed its 10-year activities including the additional programs in April 2001. The achievements of this project during the period have resulted in the accumulation of massive amounts of important data covering exposed radiation dose measurement, thyroid examination, blood tests and other related domains. This result is not only useful for the health and welfare of the residents in the affected areas, but also will serve as globally important lessons about the effects of radiation on human health.

We owe a great deal to the support extended by the Ministries of Health and the State Agencies of Health of the Ukraine, Belarus and the Russian Federation and especially to the devotion of the staff in charge of the examination at the five centers and to the cooperation of the residents of those respective areas. Allow me to express my heartfelt respect and appreciation to all those concerned. The contribution of the Japanese experts who voluntarily took part in on-site training is also to be especially noted, and I am deeply grateful to each of them. Last but not the least, to close this keynote address, I sincerely hope that all the programs mentioned above have achieved their original objectives, which were to provide support for the three Republics in their efforts to supply the best possible medical care for the benefit of the people affected by the Chernobyl accident.

References

[1] S. Yamashita, K. Fujimura, M. Hoshi, Y. Shibata, A Report of the First Chernobyl Sasakawa Medical Symposium, Sasakawa Memorial Health Foundation, Tokyo, 1993 (In Russian, English and Japanese in separate volume).
[2] S. Yamashita, K. Fujimura, M. Hoshi, Y. Shibata, A Report on the 1993 Chernobyl Sasakawa Project Workshop, Sasakawa Memorial Health Foundation, Tokyo, 1993 (In Russian and English in one volume).
[3] S. Yamashita, K. Fujimura, M. Hoshi, Y. Shibata, A Report on the 1994 Chernobyl Sasakawa Project Workshop, Sasakawa Memorial Health Foundation, Tokyo, 1994 (In Russian and English in one volume).
[4] S. Yamashita, K. Fujimura, M. Hoshi, Y. Shibata, A Report on the 1995 Chernobyl Sasakawa Project Workshop, Sasakawa Memorial Health Foundation, Tokyo, 1996 (In Russian and English in one volume).
[5] S. Yamashita, Y. Shibata (Eds.), Chernobyl: A Decade, Proceedings of the Fifth Chernobyl Sasakawa Medical Cooperation Symposium, Kiev, Ukraine, 14–15 October 1996, Elsevier, Amsterdam, 1997.

International Congress Series 1234 (2002) 7–17

Radiation accidents: medical effects and radiation protection experience

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Keywords: Radiation; Accidents; Protection

A wide range of work elaborated by Japanese specialists in collaboration with medical practitioners of Russia, Belarus and Ukraine was based upon the thoroughly prepared research program of high statistical confidence, which was elaborated under the single methodology and quality assurance of studies. It follows to the conclusion that the Sasakawa Project is one of the most fundamental ones if results and conclusions are considered.

The goal of the present paper was to generalize research and practical experience of radiation accidents at the former USSR together with their medical effects and human protection countermeasure efficiency.

Basic postulates of UNSCEAR, ICRP and national bodies engaged in the protection of professionals and population in case of radiation accidents (and large scale radiation accidents, essentially) can be briefly formulated as follows:

(a) the deterministic effects have to be excluded;
(b) the induction of stochastic radiation effects has to be as low as possible, taking into account social and economical options.

The regular requirements on the prevention of deterministic (most severe) early effects of the accidental irradiation determine the provision of the preventive and immediate medical assistance, which is the integral component of the comprehensive measures of technical, economical and social policy character. Our experience confirms the statement that high efficiency of measures at early phase of the accident and,

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PII: S0531-5131(01)00590-8

partially, at intermediate accidental phase will significantly determine the followed frequently insignificant efficiency of measures of the mitigation of accidental stochastic effects.

The deterministic and stochastic effects of radiation accidents can be considered for the radiation accidents that happened in the former USSR.

According to 50-year data of the Registry of the Institute of Biophysics of the Ministry of Health of Russia (information until 2001), the accidents that happened in the former USSR and Russia specifically have the following features: (1) 175 radiation accidents and incidents of the relatively local character have happened; (2) three large-scale radiation accidents have happened in Techa river (1949–1952), Mayak Combine (1957) and Chernobyl Nuclear Power Plant (NPP) (1986); (3) the population has been irradiated due to the first nuclear explosion at the Semipalatinsk test site (1949).

The following induction of deterministic radiation effects in humans is specific to these events, as shown in Table 1, where data are shown for acute radiation injuries that resulted from (1) radioisotope installations and radiation sources; (2) X-ray machines and accelerators; (3) nuclear reactor incidents including criticalities; (4) nuclear submarine accidents and the Chernobyl accident shown separately for comparison. This table shows data of 568 victims with clinical (deterministic) symptoms observed. Victims (344 out of 568) have been diagnosed to have acute radiation sickness (ARS) of different severity grades. Thirty-nine percent (134 ARS cases) of these patients were victims (so-called "accident witnesses") of the Chernobyl disaster; 25% were the victims of submarine accidents; 21% were the radiation workers of the atomic industry;[1] 14.5% were people overexposed due to the accidents with radioisotope sources and other casualties.

Table 1 shows that all cases of local radiation incidents (including the wide spectrum of the specific casualties) are specific to each of several victims (and less than 10 victims, usually). At the same time, the submarine accidents cannot be considered as local ones. The specific features of sailor activities inside the nuclear submarine (closed compartments, autonomy of sailing) has determined the significantly higher scale of radiation damages that occurred in only two accidents (the combined radiation pathology was found in 133 persons including 85 ARS cases). It should be noted that about 600 persons were in the site of the Chernobyl NPP at the time of the accident (firemen are included).

Actually, ARS has developed in each fifth witness of the accident. All these patients have been exposed to acute gamma and beta radiation emitted by short-lived radionuclides and to powerful flows of gamma radiation from the destroyed reactor at the first hours after the disaster.

A total of 71 fatalities were observed at the first 3 months after the accidental irradiation of 344 ARS patients (20.6% early fatality percentage). These fatalities have resulted in life incompatible severe damages (including combination of ARS and LRI). Twenty-three percent of these fatalities were victims of radioisotope source accidents, 17% of these fatalities were victims of two submarine accidents, 18% of these fatalities (13 cases) were

[1] Deterministic effects of NPP personnel were observed at the Chernobyl NPP only.

Table 1
State Research Center-Institute of Biophysics Registry data on radiation accidents and incidents at the territory of the former USSR (as of 15 March 2001) and the number of acute radiation sickness (ARS) and local radiation injury (LRI) victims

Incident classification	Number of incidents	Number of victims with clinical symptoms (ARS+LRI)		
		Subtotal	Including those with ARS	Including those who died
(1) Incidents with radioisotope devices and radiation sources (total)	88	163	45	16
^{60}Co	17	28	15	3
^{137}Cs	19	59	13	9
^{192}Ir	34	50	10	1
Other gamma emitters	8	10	2	–
Gamma and beta emitters	2	2	–	–
Beta emitters	8	14	5	3
(2) X-ray devices and accelerators	38	39	1	–
X-ray devices	26	26	–	–
Electron accelerators	9	10	1	–
Proton accelerators	3	3	–	–
(3) Reactor incidents and criticality accidents (subtotal excluding 1986 Chernobyl accident)	34	83	73	13
Criticality accidents	16	42	42	10
Reactor incidents (other causes)	18	41	31	3
(4) Nuclear submarine accidents	4	133	85	12
(5) Other incidents (subtotal)	11	16	6	2
Subtotal (excluding 1986 Chernobyl accident)	175	434	210	43
(6) 1986 Chernobyl accident	1	134	134	28
Total	176	568	344	71

*Excluding LRI cases at Mayak PA in 1949–1956, which are not included in SRC-IBP Registry.

victims of local accidents in the atomic industry and research, and almost 40% of these fatalities (28 witnesses) were victims of the Chernobyl accident.'[2]

In analyzing the medical effects of three large-scale radiation accidents in the former USSR, it should be noted that ARS and LRI cases were not observed (excluding the Chernobyl accident witnesses) in: (a) recovery workers (should not be mixed with the accident witnesses!) and population; after the Chernobyl accident; (b) Techa river population and (c) population of the South Urals Radioactive Trace (SURT) where radiation occurred after the thermal chemical explosion of a capacitor tank of high-activity radioactive waste at the Mayak Combine (1957).

[2] Fourteen ARS survivors have died within 14 years by different causes of death (heart insufficiency, liver cirrhosis, lung tuberculosis, etc.) including three cases of myelodysplastic syndrome and acute myeloid leukemia).

Despite the formal consideration of nuclear weapon tests as non-accidental events, we think that there is the possibility of ARS incidence in some people of the Uglov area in the Altei region, taking into account that a rather high intensity of the radioactive fallout exposure inside the passage trace of radioactive clouds resulted from the first nuclear test at the Semipalatinsk test site in 29 August 1949.

Unfortunately, at the present time, the medical documents indicating this assumption are not available due to a number of reasons: people were not warned of the possible hazard, any protective countermeasures were not taken, and medical examinations were not done within 40 years after the explosion. However, the retrospective assessments of average individual effective doses and collective doses of people of this area [1,2] indirectly confirm this assumption. Actually, the assessed average individual cumulative dose was in the range of 800 mSv of acute–subacute irradiation, resulting probably from gamma and beta radiation emitted by short-lived radioactive products of the nuclear blast. It is obvious that actual variations of individual doses versus calculated averages could be five times higher at least.

This finding means that such radiation exposure could induce acute radiation pathology.

Table 2 sums up our data on individual and collective doses of different population cohorts exposed to large-scale radiation accidents and nuclear weapon test (1949) at the territory of the former USSR [2].

Table 2
Collective doses of specific population cohorts: radiation accidents and nuclear weapon tests in the former USSR [2]

Event	Regions	Population number ($\times 10^3$)	Time period	Collective dose (man Sv$\times 10^3$)	Average individual dose (mSv)
1949 Nuclear explosion	Altei region, three southwest areas	200	1949–1992	28[a]	142
	Uglov area	21.4	1949–1992	16.5[a]	800
Urals accidents	Techa river	28.1	1950–1994	6.0[b]	210
	SURT	24.0	1957–1994	1.5[a]	60
Chernobyl (population)	Strict control areas	273.0	For 70 years from 1986	23.7[c]	87
	Nine most affected regions including strict control areas	15 600.0	For 70 years	192[c]	12.3
Chernobyl (recovery workers)	1986 Recovery workers	117.4[d]	Work period	9.34	80 mGy
	1987 Recovery workers	109.6	Work period	5.1	47 mGy

[a] Ninety percent dose accumulated for the first year.
[b] Ninety percent dose accumulated for 5–6 years.
[c] Upper estimates.
[d] About 5% of recovery workers have been exposed to ≥ 0.25 Gy.

Table 2 shows the most intensive irradiation of 21 000 people of the Uglov area in the Altei region (D_{av} ~ 800 mSv, D_{coll}—16.5×10^3 man Sv), as well as the population (28.1 thousand of people) lived at Techa river (D_{av}—210 mSv, D_{coll}—6.10^3 man Sv). More than 40 years of studies elaborated by the Institute of Biophysics (affiliated branch no. 4, basically, the present name is Urals Research Practical Center of Radiation Medicine) have demonstrated that this irradiated population of Techa river upper stream was recorded and described for the first time to show cases of so-called "chronic radiation disease" (ChRD), which is the obvious radiation-induced deterministic pathology [3,4].

Detailed medical dosimetric studies have demonstrated that about 37% of ChRD patients had red bone marrow cumulated doses of more than 0.5 Gy; 27% of these patients had > 0.7 Gy doses and 18% had from 1 to 4 Gy doses.

The repeated verification of ChRD diagnoses has demonstrated that at least 66 patients had well-substantiated ChRD diagnosis [3].

Thus, medical effects of all radiation accidents that happened in the former USSR within the last 50 years (excluding nuclear weapon tests) result in the following conclusion. The deterministic radiation effects of acute radiation sickness and chronic radiation disease were observed in more than 400 victims and combination with local radiation injuries was found in more than 600 victims. (These numbers do not include about 2000 chronic radiation disease cases among radiation workers of the Mayak Combine, who were exposed to high radiation doses at the start-up period of the new radiation technologies).

Somatic stochastic effects of the three large-scale radiation accidents are summarized below.

1. Techa river

(a) At the period of 1956–1994, 16.9 thousand of the irradiated people were recorded which showed 50 leukemia cases. The excess value (21 cases) is 40%. It should be noted that in case of red bone marrow doses of > 0.5 Gy, the leukemia excess is above 60%. The increase of leukemia mortality rate has been established for people of average red bone marrow dose of > 0.7 Sv [3].

(b) The number of the excessive fatal solid cancers (in the whole irradiated cohort) is 30 cases or 3.1% as compared to the observed value (969 cases, 6.41×10^5 man years). It should be noted that the increase of fatal cancer incidence was found for cumulated doses of > 0.5 Gy, which is similar to the leukemia findings.

Because the leukemia input to the general mortality rate was not predominant and the increase of radiation-induced solid tumor incidence rate was insignificant, the decrease of the life span of the irradiated population was not found at the late periods of the observation [3,4].

Calculated values of the absolute risk of leukemia in Techa river irradiated population cohort is 0.85 (0.24–1.45) (per 10 000 man years/Gy) for 90% confidence, which is practically 3.5 times lower than that in LSS cohort [2.94(2.43–3.49)]. Obviously, this fact regularly confirms the importance of the reparation process in the case of chronic irradiation to the relatively low doses and dose rates as compared, for instance, to momentary exposure to high dose rates that existed in Japanese LSS cohort. Thus, for the discussed situation, the DDREF coefficient was 1.75 times higher than that adopted by ICRP (DDREF=2) [5]. According to Ref. [6], the replacement of the numerical value of this coefficient from 2 to 3 means that the current risk assessments are overestimated for 50% and they are overestimated for 75% if DDREF obtained for Techa river materials is accepted [3,4].

2. South Urals Radioactive Trace (SURT, 1957)

According to generalized results of 30-year surveillance of different population groups exposed at SURT [4,7,8], the excessive oncological mortality was not revealed including the one by leukemia, which can be associated to the accidental radiation. Obviously, to obtain final data and to take into account solid tumor latency, the longer and more thorough observations are necessary (essentially in two evacuated cohorts of 2300 of people exposed to the relatively higher doses).

It should be noted that cohort retrospective study was performed by four groups of exposed population, taking into account the dose values and period of the relocation, when the comparison group was composed of non-irradiated population of the Chelyabinsk region. Evacuated population was divided into three groups of average effective doses of 496 (150–1500 mSv), 120 and 40 mSv, respectively; the permanent residents (non-relocated people of SURT) had 30 years cumulated effective dose of 58 mSv.

Calculated assessments of Buldakov [4,8] have demonstrated that the additional input of probable death resulted from radiation-induced malignancies in the whole SURT population versus spontaneous mortality that can be assessed at the level of 0.94–1.27% whereas for most exposed people (2.3 thousand), it is at the level of 12–16%.

3. Chernobyl accident

Table 3 shows calculation assessments of the prognosis of life span incidence of malignant solid fatal tumors (excluding thyroid tumors in children). The prognostic values are in the range of 3% (strict control zone) to 0.3% of spontaneous rate. In Ukraine, Belarus and Russia, about 2000 thyroid cancers were recorded until 2000.

The brief description of doses and effects in Chernobyl accident recovery workers is given below. It is known that the dose verification problem is one of the most complex problems for recovery workers. A number of publications are devoted to this subject. Table 4 shows standardized assessments for 1986–1987 recovery workers that were done by Ilyin et al., Ivanov et al. and UNSCEAR (2000). Table 4 demonstrates that average values of individual and collective doses have two times maximum difference. Correspondingly, the prognostic values of life span incidence of leukemia and solid tumors are in the same range. UNSCEAR has adopted the value of the average individual dose of 1986–1987 recovery workers to be 100 mGy. This value is within assessments done by Ilyin and Ivanov (see Table 4) and apparently, it is applicable for approximate calculations. Thus, the conclusion on prognostic somatic stochastic effects in 1986–1987 recovery workers can be drawn from the upper and lower limits of assessments and averaged values

Table 3
Effective cumulated doses and predicted incidence of fatal cancer (non-threshold concept) in population after the Chernobyl accident

Areas and regions delineated by 37 kBq/m²	Number of people (×10⁶)	Collective dose (man Sv×10³)	Seventy years average effective dose (mSv)[a]	Percentage of natural background (210 mSv)	Predicted number of cancers	Spontaneous cancer number	Percentage of spontaneous cancer number
Strict control areas of nine regions of the former USSR	0.273	23.7[b]	87	41.4	1185	38 220	3.1
Nine regions excluding strict control areas of nine regions of the former USSR	15.3	168.3[b]	10.9	5.20	8415	2 142 000	0.4
Ukraine (37 kBq/m²)[c]	2.4	20.0	8.3	3.95	1000	336 000	0.3
Former USSR (37 kBq/m²)	7.2	70.0	9.9	4.60	3500	1 008 000	0.35

Fatal cancer spontaneous incidence rate is $2\times10^{2}\times1\times10^{-5}\cdot\text{year}^{-1}$. Life span risk coefficient is $5\times10^{-2}\cdot\text{Sv}^{-1}$ [5].

[a] Excluding thyroid dose (effective dose is applicable to stochastic effect probability assessment and only for absorbed doses far below the deterministic effect threshold).

[b] Upper estimates (1990).

[c] From Ref. [14].

of radiation-induced effect rates, which are within ~20% of spontaneous rates for leukemia and 5–6% of solid tumor spontaneous rate (see Table 5).

Thus, the analysis of somatic stochastic effects of three large-scale radiation accidents gives the opportunity to conclude that 30–40 years of clinical epidemiological studies have established the excess rate of radiation-induced leukemia in the Techa river population (within 40% of excessive cases out of 50 cases recorded). At the same time, SURT people (35 years surveillance) and people living in Chernobyl contaminated areas

Table 4
Average individual and collective doses of external exposure of recovery workers

Year of employment	Number of people	Individual doses (mGy)			Collective doses (man Gy ×10³)		
		Source[a]			Source[a]		
		1	2	3	1	2	3
1986	117299	80	168	–	9.4	19.7	–
1987	109601	47	93	–	5.1	10.2	–
1986–1987	226900	64	130	100	14.5	29.7	22.7

[a] (1) L.A. Ilyin, et al., Radiation Biology and Radioecology, 35 (6) (1995) (in Russian). (2) V.K. Ivanov, et al., Outline: radiation related cancer from the Chernobyl accident. 50th session of UNSCEAR, 23–27 April 2001. (3) UNSCEAR 2000 Report, Annex J. Exposures and effects of the Chernobyl accident, UN, New York, 2000.

Table 5
Predicted life span risk of fatal leukemia and solid tumors in 1986–1987 recovery workers according to external gamma doses

Number of 1986–1987 recovery workers	Leukemia (%spontaneous rate)				Solid tumors (%spontaneous rate)			
	Source[a]			Average	Source[a]			Average
	1	2	3		1	2	3	
226 890	13.8	21.5	28.1	21.1	3.5	5.4	9.1	6

Leukemia spontaneous rate is $5\times1\times10^{-5}\cdot\text{year}^{-1}$; solid tumor spontaneous rate is $2\times10^{2}\times1\times10^{-5}\cdot\text{year}^{-1}$. Life span risk coefficients of radiation workers are: $4\times10^{-3}\cdot\text{Sv}^{-1}$ (leukemia) and $4\times10^{-2}\cdot\text{Sv}^{-1}$ (solid tumors). Life span under risk is 37 years.

[a] See Table 4.

(14 years surveillance) were not found to have the increase of leukemia morbidity that could be associated to radiation. There are considerations supporting the assumption of the absence of the epidemiologically detectable increase of this pathology in the future. The 1986 recovery workers (data of Russian State Medical Dosimetric Registry) were found to have the short time increase of leukemia morbidity at year 3 after the accident in 1996. If the non-threshold concept is accepted, then the theoretical prognosis of the excessive incidence of this pathology for the whole life span would be about 23% [9]. According to our assessments, this value will be in the range of less than 15%.

Solid tumors: According to epidemiology studies at Techa river, the excessive increase of 3% above spontaneous rate was established for fatal cancers. Theoretical assessments of the prognostic radiation-induced fatal cancer incidence in SURT population and Chernobyl strict control area zones are in the range of 1–5%, similar to the recovery workers [2,4,9]. As in 2000, the actual increase of the morbidity and mortality was not detected for malignant tumors in people of categories noted above, which is confirmed by research studies and statistical reports of the healthcare authorities.

This conclusion is also valid for the current indices of general mortality of population and recovery workers.

Based upon these assessments indicating very low values of the prognostic rates of radiation-induced solid cancers as compared to the spontaneous rate, one can assume that even the large-scale epidemiological studies (including adequate controls) can hardly provide retrospective actual data confirming the prognostic assessments. This conclusion is also supported by publications devoted to the analysis of the necessary quantity of statistically confident data able to reveal radiation carcinogenic effect of low radiation levels (see Table 6).

On the background of these conclusions, the clearly expressed excess of the thyroid malignant tumor incidence was established in persons, who were in their childhood at

Table 6
The size of sample required to assess dose-effect ration for carcinogenesis (90% confidence probability) [10]

Dose (Sv)	Sample size (number of people)
1	1000
0.1	100 000
0.01	10 000 000

the time of Chernobyl accident, and in the 1986 recovery workers (data of Russian State Medical Dosimetric Registry).

The radiobiological explanation of this phenomenon consists in high thyroid doses and dose rates that resulted from the "iodine impact" of Chernobyl. For instance, it should be mentioned that average thyroid absorbed dose in children (ages below 7 years) in rural areas of Gomel region was up to 1 Gy [11]. Apparently, it can be accepted that these are deterministic–stochastic effects of thyroid damage resulting from the relatively short-time (1–2 months after the accident) acute–subacute irradiation from thyroid incorporated radionuclides of iodine.

This circumstance that resulted in major radiological effects is the specific feature of the Chernobyl accident, which is different from events in Techa and SURT. At the same time, all three accidents are specific to chronic whole-body low-dose rate exposure to long-lived radionuclides. Levels of this exposure are generally the same as the life span doses resulted from the natural background radiation. In the framework of philosophy of assessments and prognosis of radiological (stochastic) effects of chronic exposure at the population level, the concept of so-called "practical threshold" for the induction of such effects is shared and supported [1,2,12] by authors of the present paper. The adoption of possibility of such threshold levels, where stochastic effects would not be realized if doses are below these thresholds, is predominantly determined by the importance of the reparative processes in the whole organism, if low-LET radiation of low intensity is under consideration. The subject of recommended numerical values of the "practical threshold" is discussible. In recent years, the necessity of the "threshold" approach is shared by more radiation protection researchers.

The de facto adoption of "practical threshold" will particularly give the opportunity to exclude the concept of "collective dose", when risks of stochastic effects are assessed for large human populations exposed to low and, essentially, super low doses equal to portions of the natural background dose; at these doses, the effects were not detected and, moreover, will not be detected (see above). Examples of such assessments are given in Table 3.

When discussing problems of protective measures to prevent deterministic effects and to mitigate stochastic effects of human irradiation in case of large-scale accidents, it is necessary to take into account the comprehensive origin of these measures. Obviously, the major goal of protective measures is the exclusion or decrease of population doses taking into account economical and social factors. It is also obvious that one of the most effective countermeasures is the population evacuation at early phase of the accident [4]. If such evacuation was delayed for days, weeks, months and even years (e.g., Techa situation), then the dose decrease efficiency would be inversely proportional to the evacuation-term or would be inconvenient. The modern approaches state that the preventive evacuation (relocation) of 28 000 people from the upper stream river area settlements could be most effective in 1949, when the release of radioactive waste to Techa river system had started.

It is also obvious that the effectiveness of protective measures at early phase and less effective measures at intermediate phase of the accident determine the scale of stochastic effects of the radiation.

Example: The absence of the operative information on terrestrial scales and levels of iodine hazard within first 2 weeks after the Chernobyl accident and the absence of the state alarm system to warn people in the European part of the former USSR, the organizational non-preparedness of correspondent authorities to provide iodine prophylaxis to people as well as other circumstances, have basically determined radiological effects related to the overexposure of the thyroid in people under the radioactive fallout.

Our experience certifies to the fact that timely and strict management of the accidental and post-accidental exposure of population and radiation workers are the most important factors to minimize radiation health effects. *Example*: The differentiated standards of population exposure at first 3 years after the accident adopted by National Commission on Radiation Protection in May 1986 have resulted to three to five times decrease.

The other purely medical aspect of protective measures consists of the problem of medication prophylaxis of the external gamma irradiation and radionuclide body incorporation. This subject is considered in monograph [13]. It should be noted that strictly differentiated indications to apply correspondent medications and means are only justified at early and, partially, intermediate phases of the accident. During the accident recovery period, when doses are basically below the established standards, the indications to the long-term application of radioprotectors seem to be absent because of their inefficiency for low doses and dose rates specific to the situations of chronic exposure. The same considerations are valid for means considered to increase the radioresistance of the organism. Moreover, the experimental evidences of their effect in the decrease of malignant tumor incidence are absent. The same conclusion is relevant to means of radionuclide excretion acceleration. Nevertheless, the "non-threshold" hypothesis predetermines the logic of such recommendations. Unfortunately, such proposals do not take into account the fact of the long-term application of such means in the case of chronic radionuclide intake. In the majority of cases, there is no experimental evidence of the biological safety of such a long-term application. Alternatively, there are a number of experimental studies confirming the fact that the relative "benefit" of the moderate decrease of doses is incomparable to the biological harm (mortality criterion) of such agents [13].

The experience demonstrates that most rational and effective system of medical assistance to population exposed to the accidental radiation is the screening based upon the differentiated approach to the irradiated individuals. The principal importance of screening management for late radiation effects consists in the separation of population groups at higher risk of carcinogenic diseases, which increases the efficiency of early diagnosis, prophylaxis and therapy of such pathology.

Finally, it should be noted that the fundamental monograph on Large Radiation Accidents: Effects and Protective Measures has been published in April 2001. This book, for the first time, generalizes the Russian experience of the discussed subject and provides the critical analysis of all population protective measures and environment protection actions applied with the specific emphasis to their adequacy, insufficiency and over-application.

References

[1] L.A. Ilyin, Radiobiology and radiation protection: problem and perspective of their interaction for radiation exposure regulation, in: The Third Congress on Radiation Research, Moscow, 14–19 October, vol. 1, (1997) 11–12 (in Russian).

[2] L.A. Ilyin, Medical Radiology and Radiation Protection Journal 43 (1) (1998) 8–17 (in Russian).
[3] A.V. Akleev, M.F. Kisselev (Eds.), Medical Biological and Ecological Effects of Techa River Radioactive Contamination, Medbioextrem, Moscow, 2000 (in Russian).
[4] L.A. Ilyin, V.A. Gubanov (Eds.), Large Scale Radiation Accidents and Protective Measures, IzdAT, Moscow, 2001 (in Russian).
[5] 1990 ICRP Recommendations, 1990, ICRP Publication 60. English–Russian Translation, Energoatomizdat, Moscow, 1994 (in Russian).
[6] F. Mettler, A.C. Upton, Cancer induction and dose–response model, in: F. Mettler, A.C. Upton (Eds.), Medical Effects of Ionizing Radiation, 2nd edn., Saunders, Philadelphia, 1995, pp. 73–112.
[7] A.V. Akleev, P.V. Goloshapov, et al., Radioactive Environmental Contamination in South Urals Region and its Population Health Effects, TcniiAtomInformm, Moscow, 1991 (in Russian).
[8] L.A. Buldakov, S.N. Demin, M.M. Kossenko, et al., Medical effects of 1957 South Urals accident, Medical Radiology and Radiation Protection Journal 12 (1990) 11–16 (in Russian).
[9] V.K. Ivanov, A.F. Tsyb, Medical effects of the accident at the Chernobyl NPP in recovery workers and population: prognosis and actual data, in: N.V. Gerasimova (Ed.), Chernobyl: 15 Years Later, Kontakt-kultura, Moscow, 2001 (in Russian).
[10] C.E. Land, Estimating cancer risks from low doses of ionizing, Science (1980) 1197–1203.
[11] L.A. Ilyin, Regulation of radiation exposure, irradiation of population and medical effects of the Chernobyl accident, Medical Radiology and Radiation Protection Journal 36 (12) (1991) 9–18 (in Russian).
[12] L.A. Ilyin, Problems of regulation of radioactive radiation and intervention levels applicable for radiation protection, Radiation Protection Problems 3 (1999) 3–16 (in Russian).
[13] L.A. Ilyin, Fundamentals of Human Protection Against Radioactive Substances, Atomizdat, Moscow, 1977 (in Russian).
[14] I.A. Likhtarev, et al., One Decade After Chernobyl Accident: Ukraine National Report, Minchernobyl, Kiev, 1996 (in Russian).

Reports from the five centers

International Congress Series 1234 (2002) 21–27

Experience in providing medical assistance to patients with thyroid diseases

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Keywords: Chernobyl; Thyroid cancer; Mogilev

1. Introduction

The Chernobyl Sasakawa Health and Medical Cooperation Project, which was conducted with the cooperation of Japanese scientists over a 10-year period, made it possible to study and implement new medical technologies for the diagnosis and treatment of patients with hematological and thyroid diseases and to statistically process the scientific data obtained from investigation results.

Regular contacts between Japanese scientists and Mogilev specialists, as well as training courses for our doctors and engineers at Nagasaki University in Japan, allowed us to enrich our knowledge and practical skills. The Sasakawa Memorial Health Foundation also extended enormous support by providing medical equipment, reagents, consumables and various scientific medical information.

One of the most serious medical problems after the Chernobyl accident was a dramatic increase in the incidence of thyroid cancer among the population of the Mogilev region. While only 58 cases of thyroid cancer were found among adults residing in the territory of the Mogilev region before 1985 as shown in Table 1, 1063 cases (including 37 children) of thyroid cancer have been diagnosed during the period of 15 years after the Chernobyl disaster. This represents an 18-fold increase in thyroid cancer. The first case of childhood

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PII: S0531-5131(01)00591-X

Table 1
Thyroid cancer in the Mogilev region in the two periods before and after the Chernobyl accident

Period	Cases	Childhood cases (0–15 years old)
1972–1985	58	–
1986–2000	1063	37
Total	1121	37

thyroid cancer was found in 1990. An increase in thyroid cancer occurred in 1993, but a dramatic increase was noted in 1998 (Fig. 1).

In comparison with other regions of the Republic of Belarus, a significant increase was noted in the incidence of thyroid cancer among the population over 19 years of age in the Mogilev region, people who were children at the time of the accident (Fig. 2). Thus, in the Mogilev region, the incidence per 100 000 population was 19.5 and 20.4 in 1999 and 2000, respectively, while in the Gomel and Brest regions it did not exceed 13.9 and 5.7 in 1999 and 2000, respectively. Since the average incidence per 100 000 population is 10.6 in the Republic of Belarus, the prevalence of thyroid cancer in adults is now highest in the Mogilev region.

We, therefore, changed the target of medical screening from children to adults after the first Chernobyl–Sasakawa Project, which had focused on the screening of school children, terminated in April 1996. In this presentation, we introduce the role and medical activities

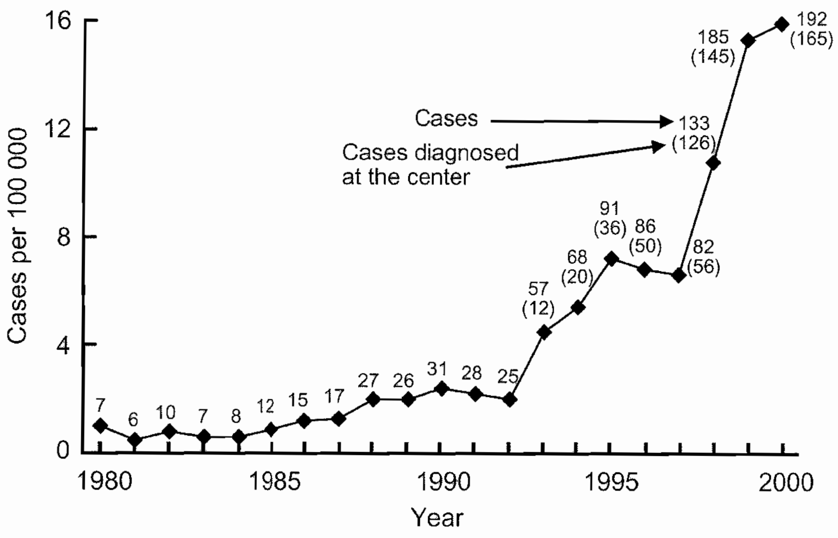

Fig. 1. Incidence of thyroid cancer among the population of Mogilev region from 1980 to 2000. The figures present the number of cases and the parenthetic entries refer to the number of cases diagnosed by the Mogilev Regional Diagnostic Center.

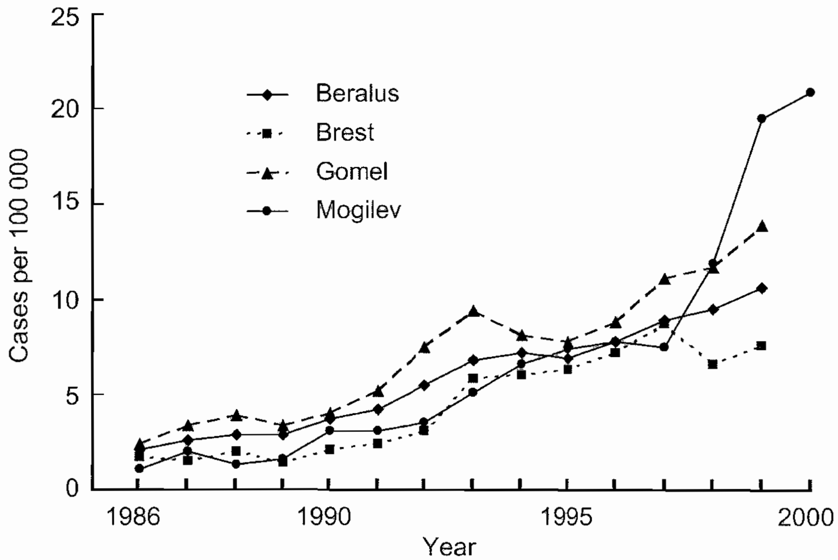

Fig. 2. Temporal trends of incidence of thyroid cancer in adults (over 19 years of age) after the accident in Belarus and the three districts of the country.

of the Mogilev Region Diagnostic Center and summarize the results of thyroid examinations conducted from 1996 to 2000.

2. Structure and methods

A step-by-step improvement of medical assistance programs for patients with thyroid diseases was conducted and organized with the support of the Sasakawa Memorial Health Foundation. The flow diagram of medical checkups for thyroid diseases is now established in the Mogilev region as shown in Fig. 3. In particular, the development of a multistep thyroid examination made it possible to improve the accuracy of thyroid disease diagnosis and contributed to the establishment of a relay system from diagnosis to treatment, especially from the Mogilev Diagnostic Center to the Republican Thyroid Cancer Center.

Owing to the medical support received from the Sasakawa Memorial Health Foundation, the following goals have now been achieved. First, thyroid ultrasound screening carried out by mobile teams has made it possible to determine high-risk groups among the radiation-exposed and general population in the radio-contaminated areas. Second, if a more extensive examination is needed, patients are consulted and referred to our center from four different routes: doctors participating in mobile diagnostic teams, physicians from local medical centers, doctors from the Diagnostic Center, and patients who come for examinations of their own volition. Third, the verification of diagnoses of thyroid diseases

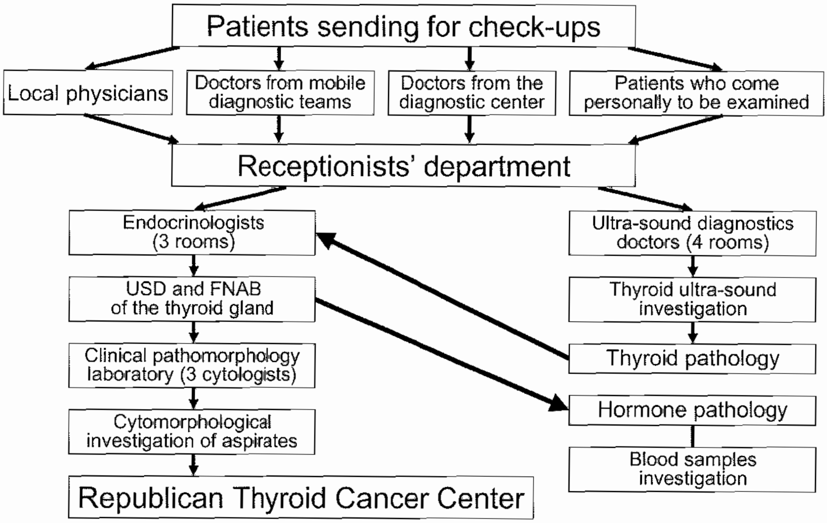

Fig. 3. Flow diagram of thyroid disease detection at the Mogilev Regional Diagnostic Center.

is now established on the basis of cytological investigations of aspirates obtained from echo-guided fine-needle aspiration biopsy (FNAB).

3. Results

The prevalence of thyroid tumors in patients diagnosed by endocrinologists from 1993 to 2000 is summarized in Table 2. Out of 177 259 patients examined, 13 838 underwent FNAB, and the cytological diagnosis indicated malignant thyroid tumor in 610 cases. A total of 542 cases (62 males and 480 females) of malignant thyroid tumor were diagnosed

Table 2
Prevalence of malignant thyroid tumor in patients diagnosed by endocrinologists at the Mogilev Regional Diagnostic Center

Year	Number of patients examined	Number of patients undergoing biopsy	Number of cases with malignant thyroid tumor	
			Absolute	Per 1000 patients
1993	10795	219	12	1.1±0.32[a]
1994	16762	562	20	1.2±0.27
1995	12460	1031	36	2.9±0.48
1996	16607	1892	50	3.0±0.43
1997	19261	2036	56	2.9±0.39
1998	28339	2377	126	4.4±0.39
1999	34989	2622	145	4.2±0.35
2000	38046	3099	165	4.3±0.33
Total	177259	13838	610	3.4±0.14

[a] Standard error.

by our center from 1996 to 2000. The data on the number of thyroid cancer cases by sex and age presented in Fig. 4 show that the largest number of cases was observed in the 41–50 years age group in both of males and females.

Various thyroid nodular lesions were found in 12026 of 137200 patients who underwent echo-guided FNAB from 1996 to 2000. Adequate materials were obtained from 72% of the sampled aspirates. Classification of thyroid diseases was carefully performed after cytological verification and all the suspected malignant tumors were eventually confirmed by histological examination at the center in Minsk.

Over the last 5 years, 542 cases of malignant tumor were found by our center. The classification of malignant tumors on the basis of cytological diagnosis is shown in Fig. 5. A total of 638 patients, consisting of the 542 cases of malignant tumor, 28 patients with follicular neoplasm and 68 patients with an indefinite cytomorphological diagnosis, were referred by specialists of our center to the Republic Thyroid Cancer Center in Minsk (Table 3). Out of 510 surgically treated patients with a cytomorphological diagnosis of papillary adenocarcinoma, the diagnosis was confirmed histologically in 502 cases (98.4%). Similarly, out of 12 surgically treated patients with a cytomorphological diagnosis of medullary carcinoma, the diagnosis was confirmed in 9 cases (75.0%). As a whole, the cytological diagnoses of malignant tumor made by our center were confirmed histologically in 97.9% of cases by the Republic Thyroid Cancer Center.

Experts recommend that the phenomenon of a high incidence of thyroid cancer be followed up carefully for many years. The increases observed in lymphatic and hematogenic metastasis remain to be elucidated, a problem that causes considerable concern among our medical staff. It is imperative that we organize an adequate system of medical assistance for those whose health has been affected by the accident. At the same time,

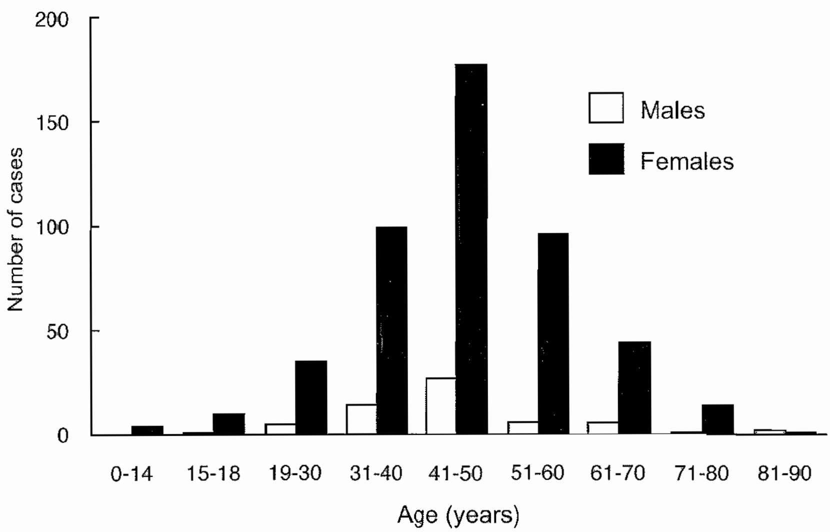

Fig. 4. Number of thyroid cancers by sex and age diagnosed by the Mogilev Regional Diagnostic Center from 1996 to 2000.

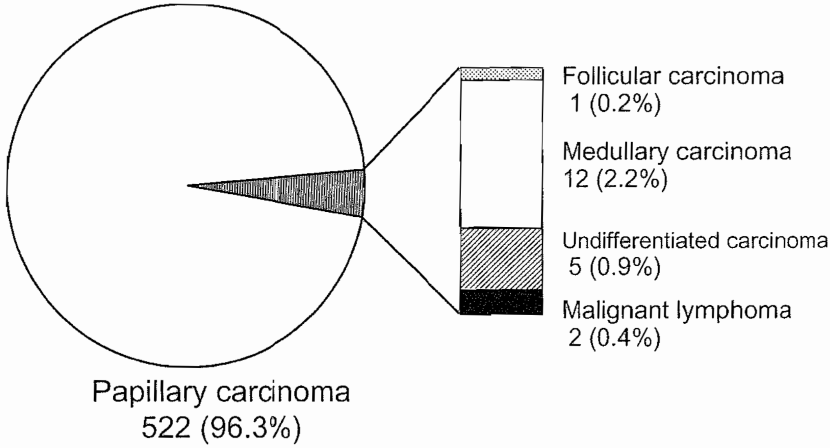

Fig. 5. Classification of 542 malignant thyroid tumors diagnosed on the basis of cytology by the Mogilev Regional Diagnostic Center from 1996 to 2000.

however, the resources allocated by our government are clearly insufficient. The current economic situation in the Republic of Belarus simply does not allow proper medical attention to the people exposed to the Chernobyl accident.

Table 3
Cytological diagnosis at Mogilev Regional Diagnostic Center and their diagnosis by the Republic Thyroid Cancer Center (RTTC) in Minsk

Diagnosis made by RTTC[a]	Cytological diagnosis							
	Papillary carcinoma	Medullary carcinoma	Follicular carcinoma	Undifferentiated carcinoma	Malignant lymphoma	Follicular neoplasm	Hyperplasia? Tumor?	Total
Papillary carcinoma	502	1				2	14	519
Medullary carcinoma		9						9
Follicular carcinoma			1			3	3	7
Undifferentiated carcinoma				1(4)				1(4)
Malignant lymphoma					(2)			(2)
Goiter	5	2				1(5)	5	13(5)
Thyroiditis	2							2
Follicular adenoma	1					5	2	8
Others								
Subtotal	510	12	1	5	2	16	24	570
Data not available	12					12	44	68
Total	522	12	1	5	2	28	68	638

[a] Based on histology (except those in parentheses, which were confirmed without surgery).

Therefore, the healthcare authorities in our region will be grateful for any additional humanitarian aid, which will contribute to the improvement of our health situation.

4. Conclusions

(1) The increase in thyroid cancer requires the establishment of an effective system of early diagnosis and continuing treatment in specialized centers in the Mogilev region.

(2) Ultrasound thyroid screening should be carried out on people exposed to the accident under 19 years of age, irrespective of place of residence.

(3) Due to the limitation of state budgets addressing health problems and minimizing the consequences of the Chernobyl accident, the establishment of a joint program of cooperation with international organizations is needed to resolve the fundamental scientific and practical problems related to the accident.

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Results of the screening of children in southwestern areas of the Bryansk region from 1996 to 2000

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Keywords: Bryansk region; Sasakawa Memorial Health Foundation; Thyroid

1. Introduction

The Bryansk Regional Diagnostic Center No. 2 was established in 1998 on the basis of the diagnostic laboratory of the Klincy City Children's Hospital, which was originally set up in 1991 within the framework of the "Chernobyl–Sasakawa" Project. The Center has received all diagnostic, auxiliary and office equipment and transport facilities from Sasakawa Memorial Health Foundation as a humanitarian aid donation. All staff members employed previously at the diagnostic laboratories are working for the Center at the present time.

The aim of the medical screening performed is to determine thyroid abnormalities in children residing in radio-contaminated areas of the Bryansk region.

2. Subjects and methods

During the period from May 1996 to the end of 2000, children from four districts in the Bryansk region, aged 5–17 years, were examined annually. A majority of the children resided in Klincy city. The examination of the children was carried out in accordance with orders of the Russian Ministry of Health and local health care authorities as part of the relevant federal program.

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PII: S0531-5131(01)00592-1

The examinations were carried out using diagnostic equipment donated by the Sasakawa Memorial Health Foundation during the period from 1991 to 1996. All diagnostic equipment is in good working condition, thanks to continuation of financial support from the Sasakawa Memorial Health Foundation. The supply of sufficient quantities of consumable materials is financed by federal and regional budgets.

Up to 1998, the approach and content of the examinations in all children were similar to those of the first Chernobyl–Sasakawa Project.

Measurement of whole body ^{137}Cs concentration in children was performed with a whole body counter (Model-101) manufactured by Aloka (Japan). Height, body weight and size of the chest were measured before the examination.

Examination of the thyroid glands included examination by an endocrinologist, ultrasound investigation and, if thyroid abnormality was suspected, determination of serum free thyroxine (FT_4) and thyroid-stimulating hormone (TSH) concentrations as well as the titers of antimicrosome (AMC) antibodies and antithyroglobulin (ATG) antibodies.

Ultrasound scanning of the thyroid gland was carried out with an arch-automatic ultrasound instrument (Aloka SSD-520). The definition of goiter is a thyroid volume exceeding the volume calculated using a certain formula. To study thyroid function, we determined the concentration of FT_4 and TSH by the immunometric diagnostic system "Immunotech" (Czechia) using "Amersham" apparatus. The titers of AMC and ATG antibodies were determined by the reaction of indirect hemagglutination using "Eritrognost" kits (Obninsk, Russia).

Thyroid volume, echogenity, presence of thyroid abnormalities, nodules, cysts, calcificates, as well as the levels of FT_4 and TSH and positive titers of AMC and ATG antibodies, were taken into consideration in the establishment of a diagnosis.

Peripheral blood tests were conducted using the hemoanalyzer, Model K-1000 and NE-7000 of Sysmex. The analysis of morphologic leukocyte differentiation was performed

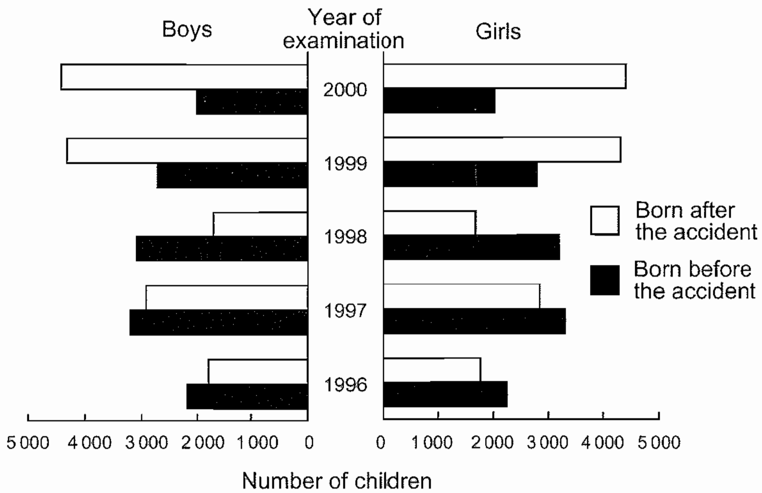

Fig. 1. Number of children examined by Bryansk Regional Diagnostic Center No. 2 from May 1996 to December 2000, by sex, period of birth and year of examination.

using an "Olympus" microscope. Peripheral blood smears were stained by the May-Grünwald-Giemsa method.

Since 1998, the examinations mentioned above have been carried out only for children born before the accident. We conducted ultrasound investigation of the thyroid and determinations of TSH and FT_4, titers of ATG and AMC antibodies only in cases in which thyroid abnormality was suspected as a result of examination by a pediatrician and endocrinologist.

3. Results

A total of 56 941 children (28 374 boys and 28 567 girls) in four districts of the Bryansk region, aged 5–17 years, were examined by Bryansk Regional Diagnostic Center No. 2 in the period from May 1996 to December 2000. The number of children examined each year is presented in Fig. 1 by sex and birth period. The number of children born before and after the Chernobyl accident was 26 767 (13 207 boys and 13 560 girls) and 30 174 (15 167 boys and 15 007 girls), respectively. The number of children born before the accident exceeded that of those born after the accident up to 1998, but the relationship was reversed in 1999 and 2000.

A total of 41 787 children underwent thyroid ultrasound examinations from May 1996 to December 2000: 28 233 were born before the accident and 13 554 were born after the accident. The number of children examined in 1996 and 1997 was similar for children born before and after the accident, while children born before the accident became dominant from 1998 onward (Fig. 2). The reason for this peculiar phenomenon is that thyroid ultrasound examinations, which were performed for all children in 1996 and 1997, have been restricted as a rule to children born before the accident by order of the Ministry

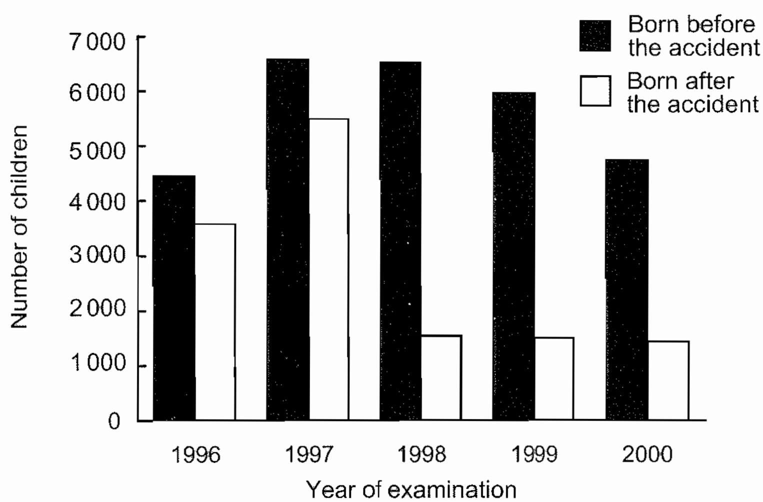

Fig. 2. Number of children who underwent thyroid ultrasonography, by period of birth and year of examination.

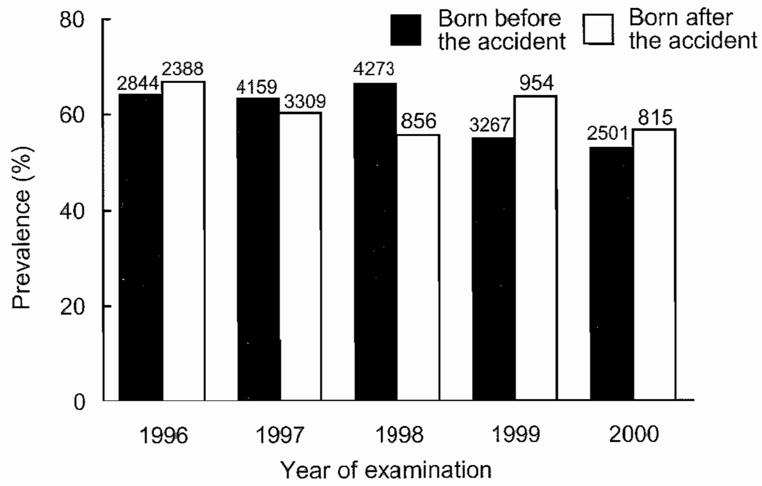

Fig. 3. Prevalence of goiter in children, by period of birth and year of examination. The numerals above the bars present the number of respective cases.

of Health. Children born after the accident undergo thyroid ultrasound examinations only if an abnormality is suspected.

Goiter was diagnosed, from May 1996 to December 2000, in 25 366 children among whom 17 044 were born before the accident and 8322 were born after the accident. The prevalence of goiter was, therefore, 60.4% and 61.4% in children born before and after the accident, respectively (Fig. 3).

Ultrasonographic thyroid abnormalities, i.e., nodules, cysts and abnormal echogenity, were diagnosed in 1273 children from May 1996 to December 2000 (Fig. 4). The

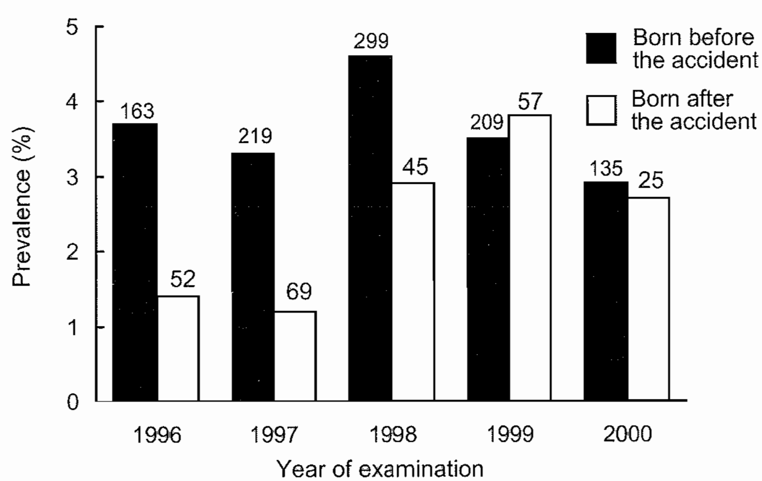

Fig. 4. Prevalence of ultrasonographic thyroid abnormalities in children, by period of birth and year of examination. The numerals above the bars present the number of respective cases.

Table 1
Thyroid cancers revealed in 41 787 children examined from May 1996 to December by the Bryansk Regional Diagnostic Center No. 2

Case	Place of residence	Sex	Year of birth	Year of examination	Histology
1	Klincy city	male	1983	1997	papillary carcinoma
2	Klincy city	male	1984	1997	papillary carcinoma
3	Klincy city	male	1985	1998	papillary carcinoma
4	Klincy city	male	1985	1998	papillary carcinoma
5	Klincy city	male	1985	2000	papillary carcinoma
6	Klincy city	female	1981	1998	papillary carcinoma
7	Klincy city	female	1981	1999	papillary carcinoma
8	Klincy city	female	1983	1999	papillary carcinoma
9	Klincy city	female	1985	1997	papillary carcinoma
10	Klintsovskii district	female	1984	1997	papillary carcinoma
11	Klintsovskii district	female	1987	1999	papillary carcinoma

prevalence of ultrasonographic thyroid abnormalities in children born before the accident was 3.6% on average, varying from 2.9% (in 2000) to 4.6% (in 1998). It should be noted that the prevalence of ultrasonographic thyroid abnormalities observed from 1998 onward in children born after the accident is probably biased because these children underwent thyroid ultrasound examinations only in cases in which abnormality was suspected.

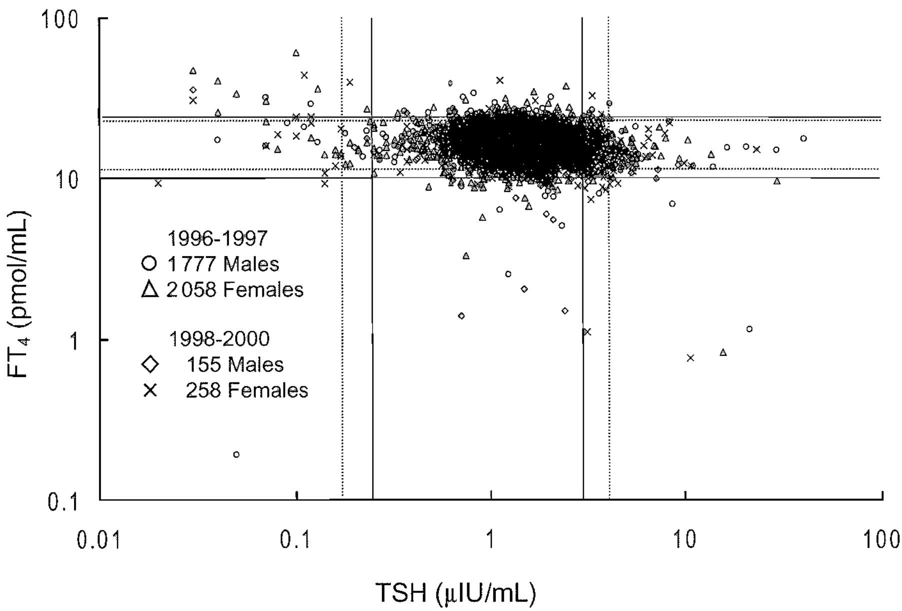

Fig. 5. Scatter plots of TSH and FT_4 levels measured for 1932 boys and 2316 girls from May 1996 to December 2000. Different kits were used in the two periods of 1996–1997 and 1998–2000. The normal limits of TSH and FT_4 in the respective periods are presented by solid lines (0.24 and 3.0 μIU/ml for TSH; 10.0 and 25.0 pmol/ml for FT_4) and dotted lines (0.17 and 4.1 μIU/ml for TSH; 11.0 and 23.0 pmol/ml for FT_4), respectively.

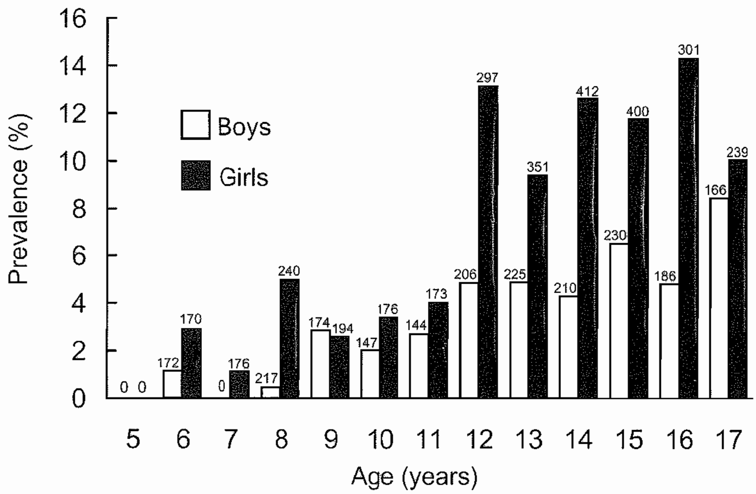

Fig. 6. The frequency of children with both positive ATG and AMC antibodies, by sex and age at examination. The numerals above the bars present the number of respective cases.

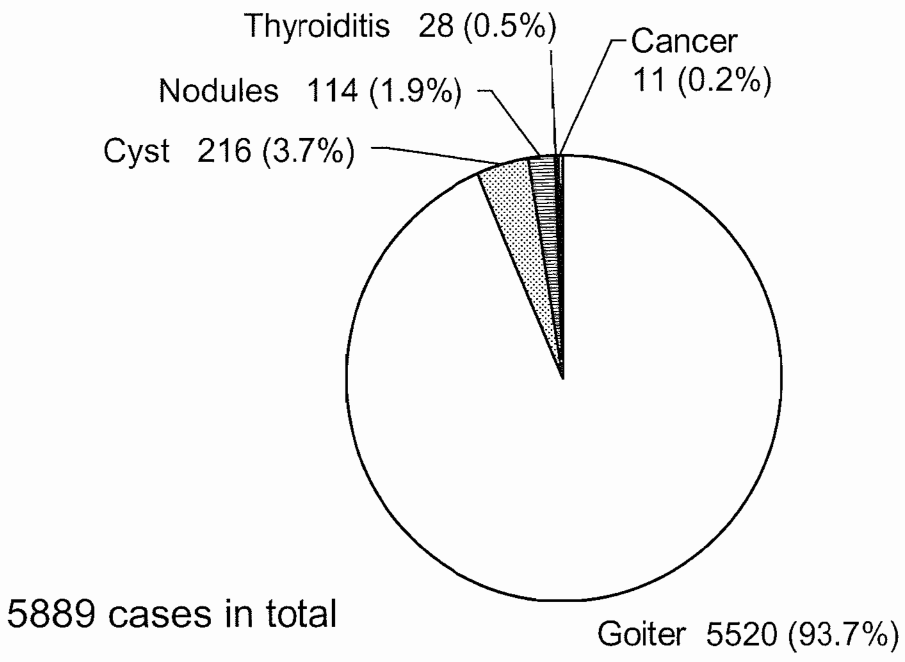

Fig. 7. Classification of thyroid diseases revealed for 5889 children by the Bryansk Regional Diagnostic Center from May 1996 to December 2000.

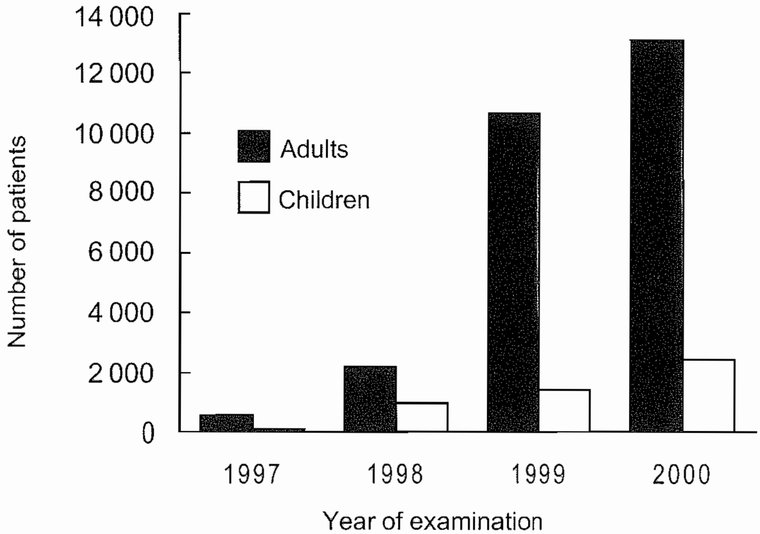

Fig. 8. The annual number of adults and children with thyroid abnormalities referred to the Bryansk Regional Diagnostic Center No. 2 by medical institutions in the districts of the Bryansk region severely affected by the Chernobyl accident.

Out of 41 787 children examined from May 1996 to December 2000, 11 thyroid cancers were revealed from 1997 to 2000 (Table 1): all were cases of papillary adenocarcinoma. Ten patients (five boys and five girls) were born before the accident, and one was a girl born in 1987. Eight of the patients were aged 0–4 years at the time of the accident.

Fig. 5 presents the scatter plots of TSH and FT_4 levels measured for 1932 boys and 2316 girls in the two periods. Both TSH and FT_4 levels were within normal range. Hyperthyroidism was registered more frequently than hypothyroidism, but both conditions were diagnosed in only a few children. A small number of cases showing an increase only in TSH were diagnosed as subclinical hypothyroidism.

Titers of ATG and AMC antibodies were measured in 5206 children (2077 boys and 3129 girls). The frequency of children who had both positive ATG and AMC antibodies was higher in girls than in boys in all age groups and tended roughly to increase with age as shown in Fig. 6.

A total of 5889 cases of thyroid abnormality were found among children screened from May 1996 to December 2000. A breakdown of the diseases is shown in Fig. 7. Euthyroid goiter accounted for most of the thyroid abnormalities (93.7%) and was followed by cystic lesions (3.7%), nodular lesions (1.9%), autoimmune thyroiditis (0.5%) and cancer (0.2%).

From 1997 to 2000, a total of 31 326 patients (26451 adults and 4875 children) with thyroid abnormalities were referred to the Bryansk Regional Diagnostic Center No.2 by medical institutions in the districts of the Bryansk region severely affected by the Chernobyl accident. The number of visits showed a yearly increase in both adults and children, and a remarkable increase in the number of adult patients was observed in 1999 (Fig. 8).

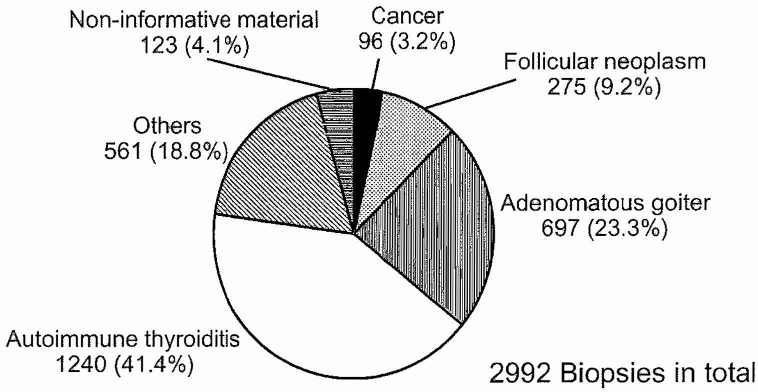

Fig. 9. Classification of cytological findings in 2992 children who underwent echo-guided fine-needle aspiration biopsy in 1997–2000.

One of the most important techniques is echo-guided fine-needle aspiration biopsy, which is performed to verify diagnoses and to provide information useful for the treatment of patients. Fig. 9 presents a breakdown of the cytological findings in 2992 children who underwent echo-guided fine-needle aspiration biopsy in the period from 1997 to 2000. Note that the cytological and histological diagnoses coincided in 97% of thyroid cancer cases (data not shown).

Whole body ^{137}Cs specific activity was measured in 41 523 children (20 557 boys and 20 966 girls). The distribution of whole body ^{137}Cs specific activity by sex and year of

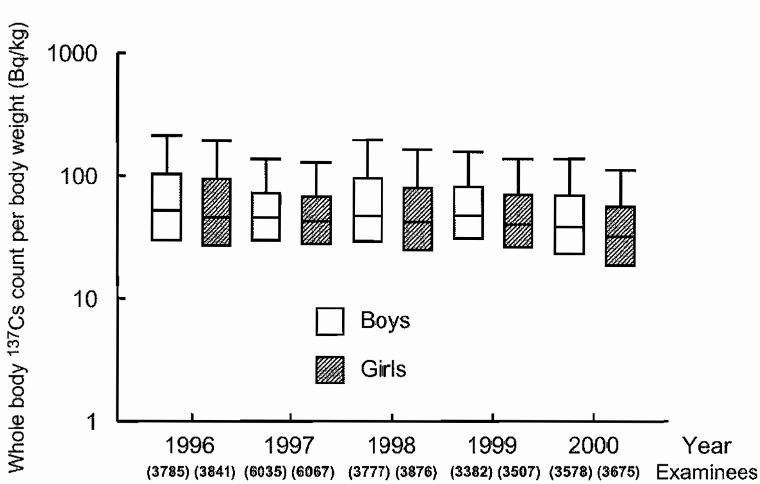

Fig. 10. The box-and-whisker plots of whole body ^{137}Cs specific activity by sex and year of examination in children residing in southwestern areas of the Bryansk region. The bottom and top ends of the box and the bar inside the box correspond to the 25th, 75th and 50th sample percentiles, respectively.

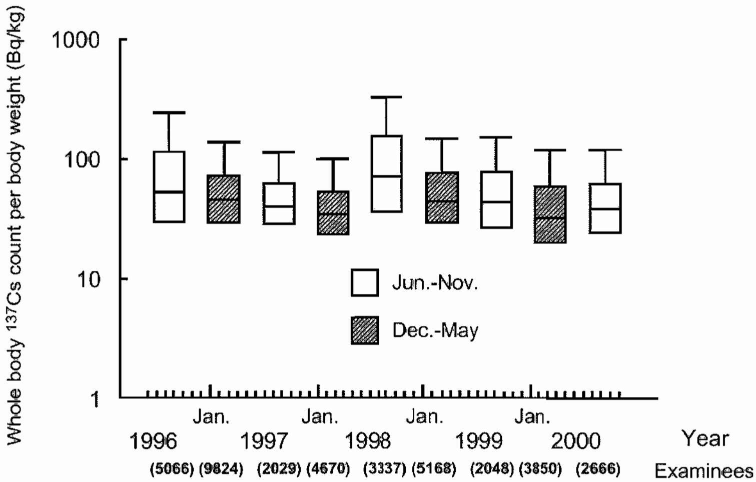

Fig. 11. The box-and-whisker plots of whole body ^{137}Cs specific activity by period of examination in children residing in southwestern areas of the Bryansk region. The bottom and top ends of the box and the bar inside the box correspond to the 25th, 75th and 50th sample percentiles, respectively.

examination is shown in Fig. 10. The median level of whole body ^{137}Cs specific activity was higher in boys than in girls throughout the period of examination and showed, though small, a temporal tendency to decrease. A seasonal variation was observed in the distribution of whole body ^{137}Cs specific activity (Fig. 11). The median level of whole body ^{137}Cs specific activity was higher in the period from summer to autumn (from June to November) than in the period from winter to spring (from December to May) through the whole periods of examination. It can be explained by the consumption in summer season of mushrooms, forest berries, fish, milk and game available in radio-contaminated areas.

4. Summary

(1) The prevalence of ultrasonographic thyroid abnormalities was higher in children born before the Chernobyl accident than in those born after the accident. The thyroid disease most frequently observed in children was euthyroid goiter, which accounted for 93.7% of cases. Cystic lesions were registered in 3.7%, nodular lesions in 1.9%, autoimmune thyroiditis in 0.5% and cancer in 0.2% of cases.

(2) Eleven cases of thyroid cancer were found from 1997 to 2000. The patients were five boys and five girls born before the accident (in 1981–1985), and one girl born in 1987. All of the cases showed papillary carcinoma.

(3) The levels of TSH and FT_4 were within normal range in most of the children and, therefore, this type of analysis should be carried out in screening only when it is indicated and economically justified. The frequency of children with both positive ATG and AMC antibodies was higher in girls than in boys in all age groups and tended roughly to increase with age.

(4) The ^{137}Cs specific activity in the body had a tendency to decrease. The ^{137}Cs specific activity was higher in boys than in girls. The ^{137}Cs specific activity during the summer and fall periods was higher than during the winter and spring. The main dose-forming factor in the population residing in radio-contaminated areas is the consumption of radio-contaminated food.

(5) For the purpose of early detection of thyroid diseases, it is necessary to perform annual screening on people born in the period of 1968–1986 and residing in the exposed territories at the time of the accident. There is no sense in performing screening without thyroid ultrasound examination.

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Recent achievements of Korosten Inter-Area Medical Diagnostic Center after completion of the Chernobyl Sasakawa Health and Medical Cooperation Project: 1996–2000

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1. Introduction

After completion of the humanitarian Chernobyl Sasakawa project in April 1996, we faced the following problems: how to keep the medical staff, the majority of whom are highly qualified specialists; how to supply reagents and consumables for subsequent use; and how to maintain the database and to preserve serum samples and hematological archives.

Geographically, the Korosten Inter-Area Medical Diagnostic Center is located close to the center of the radionuclide-contaminated area. In implementing the decisions of the Zhitomir Regional Health Care Department, which are directed toward further examinations of the population exposed to the Chernobyl disaster, the Diagnostic Center has accepted patients from the northern area of Zhitomir region, Ukraine. The patients are referred by local physicians and come with written recommendations. The Diagnostic Center is equipped with modern ultrasonic and endoscopic instruments and blood analyzers. Highly qualified specialists who participated in the Chernobyl Sasakawa Project from 1991 to 1996 are continuously working in our center. The main items of medical equipment were donated by the Sasakawa Memorial Health Foundation. The problem with shortage of reagents has partially been solved since 1997 owing to special support from the Basic Human Needs (BHN) Association in Tokyo, Japan.

2. Subjects and methods

Approximately 600 000 people including 80 000 children live in the radio-contaminated territory of the northern area of the Zhitomir region. The patients examined from 1996 to

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PII: S0531-5131(01)00593-3

2000 were subdivided into three groups: those who were adults at the time of the Chernobyl accident, those who were children at the time of the accident and those who were born after the accident.

Thyroid examinations were performed using an Aloka-630 (7.5 MHz probe) ultrasonographic instrument. Diagnoses of thyroid diseases were verified on the basis of thyroid structure, echogenity, thyroid volume and laboratory data including general blood count, hormonal status and titers of anti-thyroglobulin (ATG) antibody and anti-microsome (AMC) antibody. Physical data such as height and weight were collected as well as demographic data, including sex and age. Furthermore, functional examination of electrocardiograms (ECG) was conducted.

3. Results

The frequency of thyroid diseases diagnosed by the center in patients referred by local physicians from 1996 to 2000 is presented in Figs. 1, 2 and 3 for the three groups of patients. First, among 13 713 patients (2243 males and 11 470 females) who were adults at the time of the accident, thyroid diseases were diagnosed in 11 600 (1716 males and 9884 females) (Fig. 1). Thyroid diseases, except for diffuse goiter, were diagnosed more frequently in females than in males. Thyroid cancer was diagnosed in 15 (0.7%) males and 111 (1.0%) females. Second, among 8346 patients (2189 males and 6157 females) who were children at the time

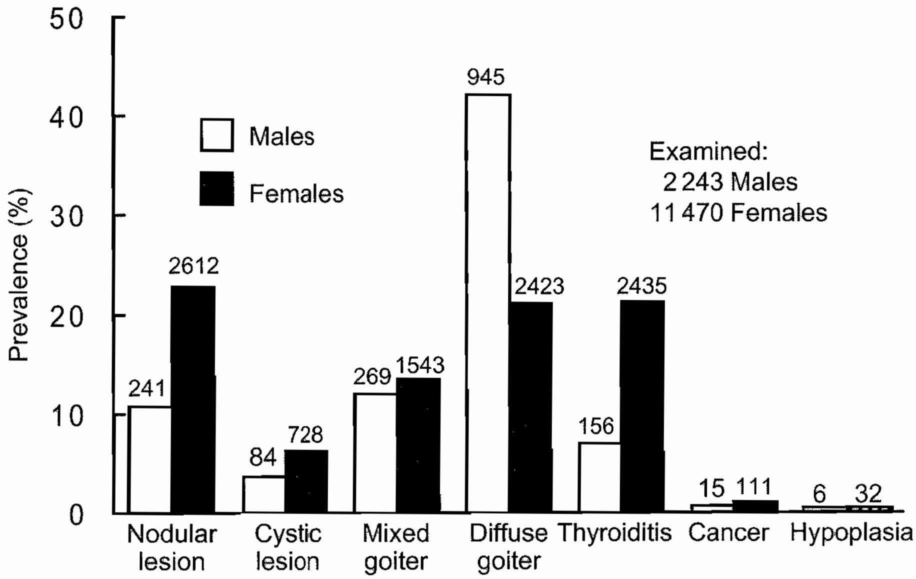

Fig. 1. Frequency of thyroid diseases diagnosed by the Korosten Inter-Area Medical Diagnostic Center among patients referred by local physicians from 1996 to 2000. The patients were all living in northern areas of the Zhitomir region of Ukraine and were all adults at the time of the Chernobyl accident. The figure on the bar indicates the number of patients diagnosed.

of the accident, thyroid diseases were diagnosed in 6164 (1555 males and 4609 females) (Fig. 2). Thyroid diseases, except for diffuse goiter, cancer and hypoplasia, were diagnosed more frequently in females than in males. Thyroid cancer was diagnosed in 4 (0.2%) males and 7 (0.1%) females. Finally, out of 2612 patients (1022 males and 1590 females) who were born after the accident, 1836 (682 males and 1154 females) were found to be suffering from thyroid disease (Fig. 3). Except for cancer, which was diagnosed in 1 male (0.10%) and 1 female (0.06%), thyroid diseases were diagnosed more frequently in females than in males. The high frequency of diffuse goiter observed throughout the three groups of patients classified by birth period is noteworthy: the frequency of diffuse goiter remained high in patients born after the accident, while the frequency of other thyroid diseases decreased to below 3.3%. This may be related to the fact that the northern area of the Zhitomir region is endemically iodine deficient.

Since 1999, we have been operating a cytological diagnostic laboratory and performing echo-guided fine-needle aspiration biopsy using an Aloka-630 (7.5 MHz probe) with a special adaptor when thyroid abnormality is suspected. The findings of biopsies conducted in 1999 and 2000 are shown in Fig. 4. Among 511 patients who underwent fine-needle aspiration biopsy, 36 (7.0%) cases of adenocarcinoma and 11 (2.2%) cases of thyroid neoplasms were diagnosed on the basis of cytological analysis. All patients with thyroid adenocarcinoma were referred to the Institute of Endocrinology and Metabolism in Kiev for surgical treatment.

From May 1996 onward, 14 thyroid cancers were found among children who had been screened in the first Chernobyl Sasakawa Project from May 1991 to April 1996 but whose

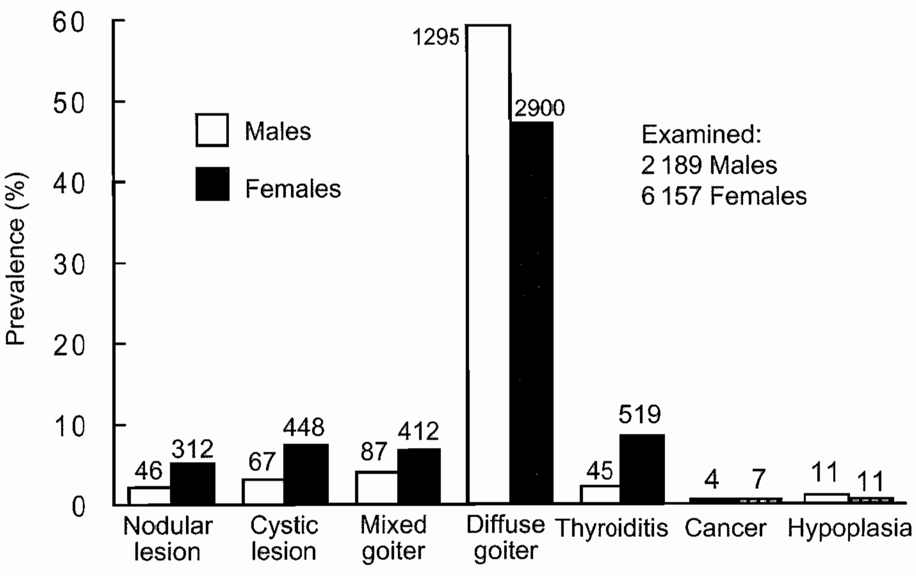

Fig. 2. Frequency of thyroid diseases diagnosed by the Korosten Inter-Area Medical Diagnostic Center among patients referred by local physicians from 1996 to 2000. The patients were all living in northern areas of the Zhitomir region of Ukraine and were all children at the time of the Chernobyl accident. The figure on the bar indicates the number of patients diagnosed.

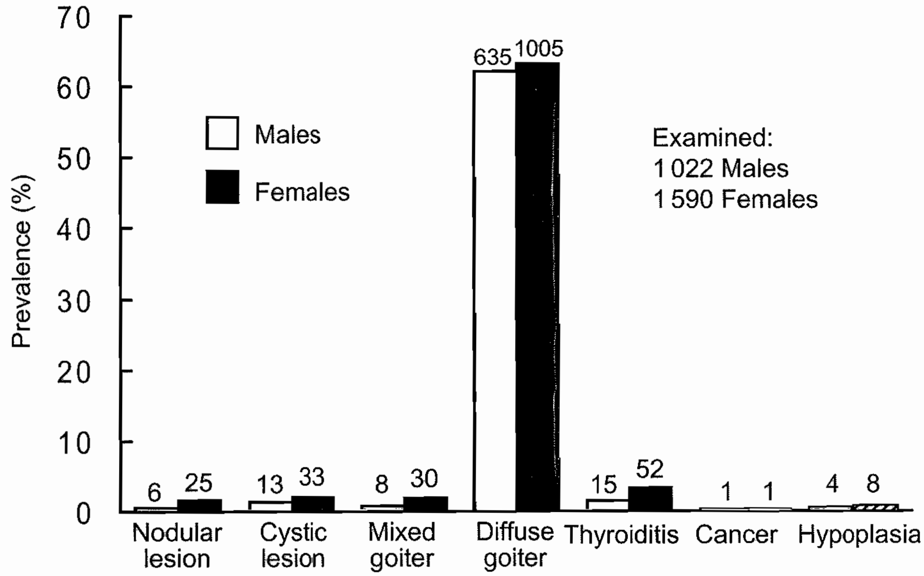

Fig. 3. Frequency of thyroid diseases diagnosed by the Korosten Inter-Area Medical Diagnostic Center among patients referred by local physicians from 1996 to 2000. The patients were all living in northern areas of the Zhitomir region of Ukraine and were all born after the Chernobyl accident. The figure on the bar indicates the number of patients diagnosed.

disease had remained undetected at that time. Among these, one girl underwent surgery for thyroid cancer in 1994 after the screening, but the information did not reach us until she visited us recently for treatment of other diseases (Table 1). The patients were from various districts in the radio-contaminated northern areas of the Zhitomir region: the surface ^{137}Cs-

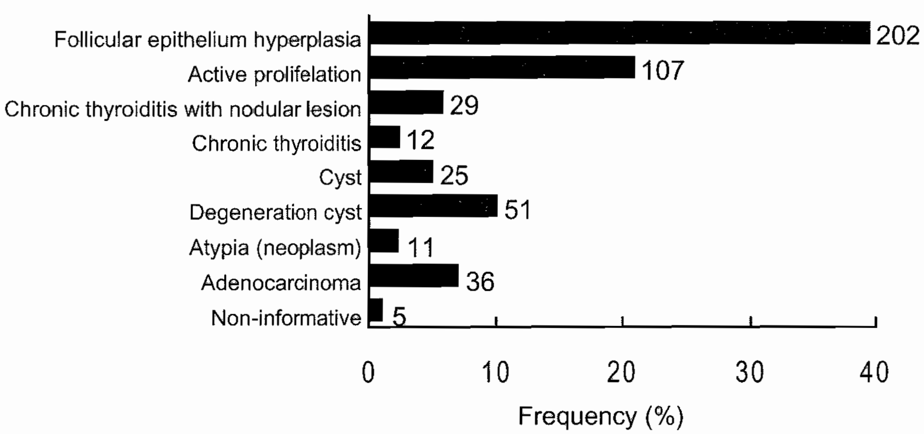

Fig. 4. Classification of cytological diagnosis in 511 patients who underwent echo-guided fine-needle aspiration biopsy by the Korosten Inter-Area Medical Diagnostic Center in 1999 and 2000. The figure adjacent to the bar indicates the number of patients diagnosed.

Table 1
Thyroid cancers found in children after the screening of the first Chernobyl Sasakawa Project carried out from May 1991 to April 1996

Sex[a]	Year of birth	District	Age at examination[b]	Thyroid volume (cm^3)[b]	Ultrasonographic findings[b]	Year of operation	Histology
F[c]	1976	Korosten city	16	49.0	diffuse goiter	1994	papillary ca.
F	1980	Luginskii	13	13.1	diffuse goiter	1999	papillary ca.
F	1980	Narodichskii	14	9.0	normal	1996	papillary ca.
F	1980	Narodichskii	14	18.5	cyst	2000	papillary ca.
F	1982	Korostenskii	10	6.7	normal	2000	papillary ca.
F	1982	Ovruchskii	13	19.5	nodular goiter	1996	papillary ca.
F	1983	Emilchinskii	12	15.2	normal	2000	papillary ca.
M	1984	Narodichskii	8	9.3	diffuse goiter	1997	papillary ca.
M	1984	Olevskii	8	3.4	normal	2000	papillary ca.
M	1984	Narodichskii	10	8.2	normal	2000	papillary ca.
F	1984	Korosten city	9	8.3	diffuse goiter	1999	papillary ca.
F	1985	Korostenskii	7	2.9	normal	1998	papillary ca.
F	1985	Narodichskii	8	6.1	nodular goiter	no operation	–
M	1986	Korosten city	8	5.5	normal	2000	papillary ca.

[a] M=male, F=female.

[b] Data at the time of the screening of the first Chernobyl Sasakawa Project.

[c] TSH=0.10 IU/ml, FT_4=47.2 pmol/l and ATG and AMC antibodies were both positive, while for the rest, TSH and FT_4 were both within normal ranges and ATG and AMC antibodies were both negative.

contamination level in Narodichskii district where five thyroid cancers were found was 15–40 Ci/km^2 in 1992. All were cases of papillary adenocarcinoma and, except for one case, all underwent surgery at the Institute of Endocrinology and Metabolism in Kiev.

The above-mentioned conditions led to a decision in 1999 to screen children in the northern areas of the Zhitomir region. A total of 5489 children (2499 males and 2990 females) in Narodichskii, Olevskii, Novograd–Volynskii and Emilchinskii districts were examined. The screening included thyroid ultrasonographic examination, determination of titers of ATG and AMC antibodies if required, general blood count and measurement of whole body ^{137}Cs specific activity. The findings of thyroid ultrasonographic examinations are presented in Table 2. The frequency of ultrasonographic thyroid abnormalities showed a tendency to increase with age in both boys and girls. Ultrasonographic thyroid abnormalities were detected more frequently in girls than in boys as a whole and this tendency was observed in the two groups of 7–13 and 14–18 years of age. The frequency observed in the group of 0–6 years of age is less reliable than that observed in the other two groups because of the small number of children examined. Thyroid cancer was diagnosed in two among 905 boys aged 14–18 years. Chronic thyroiditis was more frequently observed in girls than in boys for all age groups.

The whole body counter 101 (WBC-101) manufactured by the Aloka Company of Japan was continuously used to determine the whole body ^{137}Cs specific activity. The distribution of whole body ^{137}Cs specific activity by age in girls and boys who underwent the above-mentioned screening in 1999 is presented in Figs. 5 and 6, respectively. The distributions in the two figures showed a similar tendency, though slight, to decrease with age. The median level of whole body ^{137}Cs specific activity was between 55 and 60 Bq/kg

Table 2
Thyroid diseases detected by ultrasonography among children in northern areas of the Zhitomir region who underwent screening in 1999

Diagnosis	Age at examination (years)						Total	
	0–6		7–13		14–18		Male	Female
	Male	Female	Male	Female	Male	Female		
Thyroiditis	1(0.6)[a]		8(0.6)	28(1.8)	5(0.6)	46(3.6)	14(0.6)	74(2.5)
Cancer					2(0.2)		2(0.1)	
Cyst			7(0.5)	20(1.2)	19(2.1)	75(5.8)	26(1.0)	95(3.2)
Diffuse goiter	38(24.4)	28(22.2)	570(39.6)	713(45.2)	364(40.2)	627(48.8)	972(38.9)	1368(45.8)
Hypoplasia			2(0.1)		1(0.1)		3(0.1)	
Multi-nodular goiter						6(0.5)		6(0.2)
Mixed goiter			1(0.1)	4(0.3)	6(0.7)	20(1.6)	7(0.3)	24(0.8)
Nodular goiter			3(0.2)	7(0.4)	9(1.0)	21(1.6)	12(0.5)	28(0.9)
Normal	117(75.0)	98(77.8)	847(58.9)	807(51.1)	499(55.1)	490(38.1)	1463(58.5)	1395(46.6)
Total	156	126	1438	1579	905	1285	2499	2990

[a] Number of children with percentages in parentheses.

in all sex- and age-specific groups, but the measurements in several children exceeded 500 Bq/kg as shown in Figs. 5 and 6. No significant change was observed during the period from 1991 to 2000 in the distribution of whole body ^{137}Cs specific activity in either boys or girls (Figs. 7 and 8), a fact that suggests the continuing intake of radio-contaminated food.

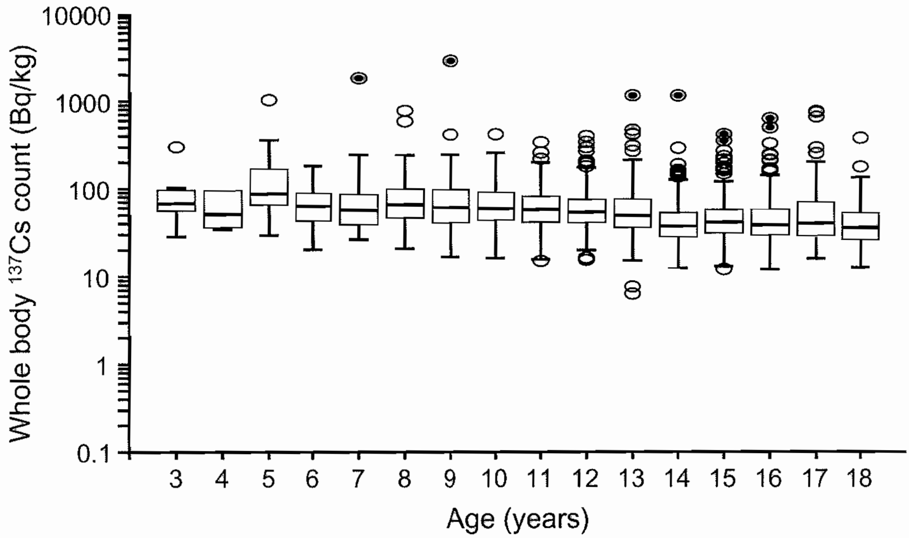

Fig. 5. The box-and-whisker plots of whole body ^{137}Cs specific activity by age in girls examined in 1999 by the Korosten Inter-Area Medical Diagnostic Center. The bottom and top ends of the box and the bar inside the box correspond to the 25th, 75th and 50th sample percentiles, respectively. The open circle and the double circle with black dot represent extreme values, called "outside" and "far out," respectively.

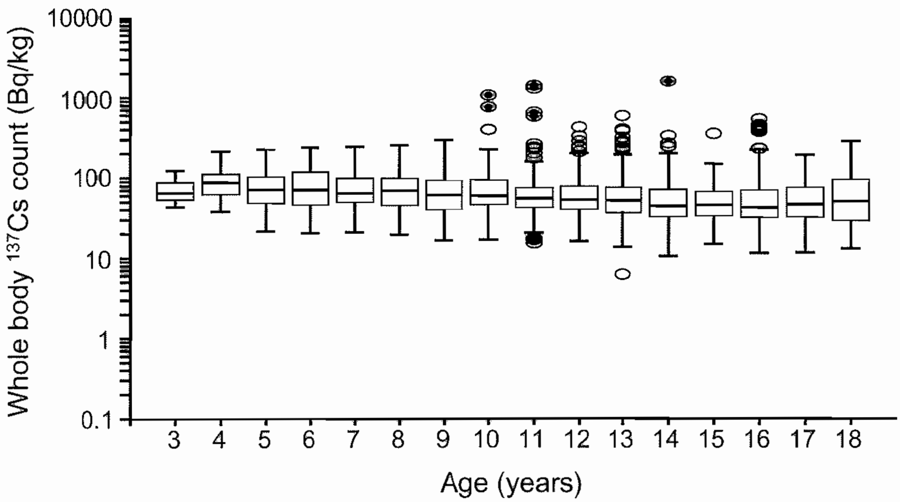

Fig. 6. The box-and-whisker plots of whole body ^{137}Cs specific activity by age in boys examined in 1999 by the Korosten Inter-Area Medical Diagnostic Center. See Fig. 5 for details of the plots.

In addition to the medical activities described above, we have to solve the very difficult problem of how to maintain the present level of medical service under the limited state budget allocated to the public health care system. The budget limitations

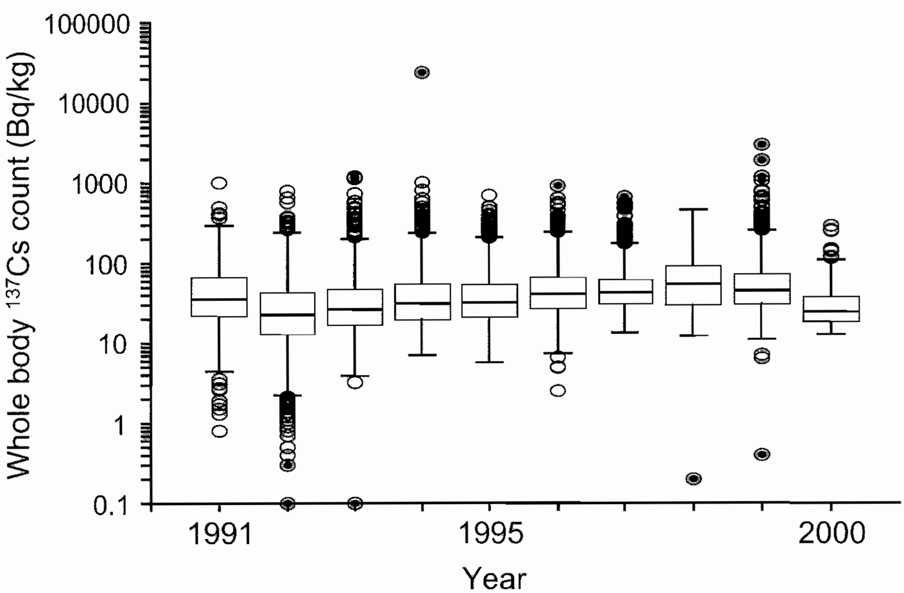

Fig. 7. The box-and-whisker plots of whole body ^{137}Cs specific activity by year of examination in girls screened in the period from 1991 to 2000 by the Korosten Inter-Area Medical Diagnostic Center. See Fig. 5 for details of the plots.

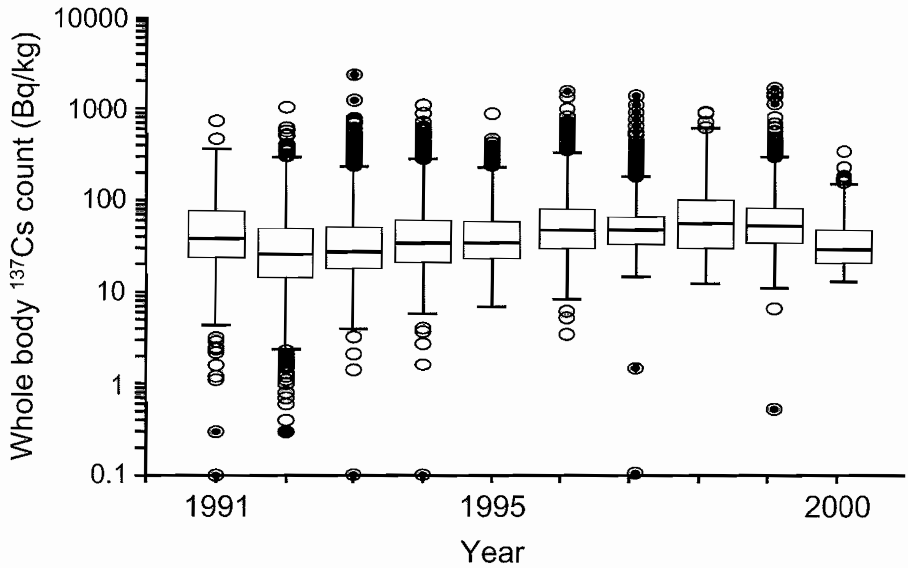

Fig. 8. The box-and-whisker plots of whole body ^{137}Cs specific activity by year of examination in boys screened in the period from 1991 to 2000 by the Korosten Inter-Area Medical Diagnostic Center. See Fig. 5 for details of the plots.

make it necessary to search for outside resources to cover the expenses of repairing medical instruments, purchasing reagents and medicines and maintaining data quality control.

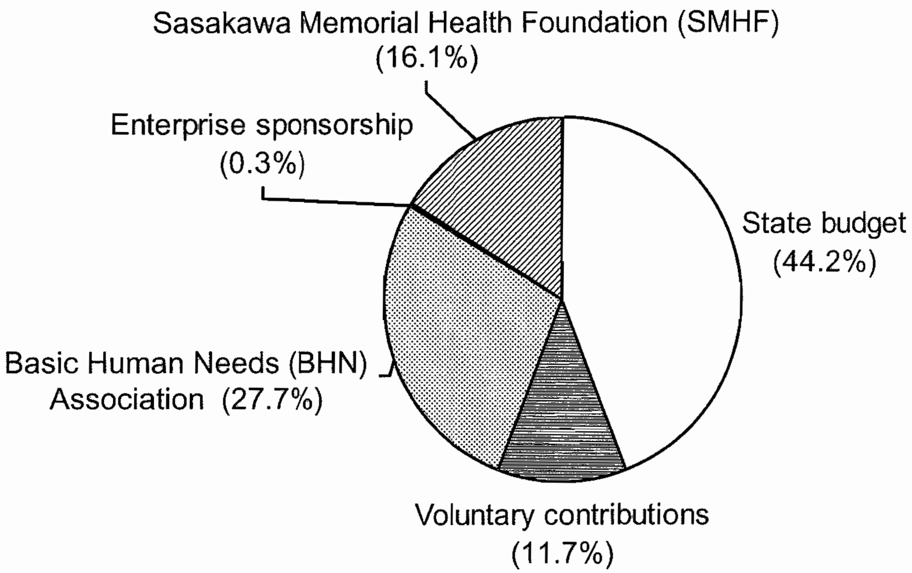

Fig. 9. Breakdown of the budget of Korosten Inter-Area Medical Diagnostic Center for the 2000 fiscal year.

One of these outside resources supporting the Korosten Inter-Area Medical Diagnostic Center is the BHN Association, which has provided funding for the purchase of reagents for K-1000 and NE-7000 blood analyzers as well as thyroid hormone (TSH and FT_4) determination, for ATG and AMC antibody kits, for clinical laboratory expenses and for consumables and instruments. Secondly, a charitable foundation has been established within our center whereby people who visit the center for examination can make donations. Furthermore, companies located in the area of our town have assisted by providing construction materials and other services to improve the departments and other rooms.

The proportion of respective contributions to the total budget of the Korosten Inter-Area Medical Diagnostic Center for the 2000 fiscal year is presented in Fig. 9. Owing to extra-budget assistance, we have managed to maintain all existing instruments and devices in good working condition and to render medical diagnostic aid to 70 000 people out of 280 000 investigated each year. The budget, however, is not enough to purchase new instruments. The Korosten Inter-Area Diagnostic Center is deeply obliged to the Sasakawa Memorial Health Foundation and the Japanese specialists who worked with us for the last 10 years and with whom we continue to keep friendly contacts. We are also grateful to the BHN Association.

4. Conclusion

(1) Our recent medical examinations of people exposed to the Chernobyl disaster indicate that thyroid examinations need to be carried out continuously for both children and adults.

(2) Special care should be given to people aged under 20 years at the time of the accident since they are considered to be at high risk for thyroid cancer over the entire life span.

(3) To solve these problems, it is necessary to keep existing financial resources and find new ones outside the state budget, because ideal thyroid examinations are very expensive.

International Congress Series 1234 (2002) 49–55

Medical screening of thyroid diseases in the Gomel region, Belarus

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Keywords: Medical screening; Thyroid diseases; Belarus

1. Introduction

The medical impact of the Chernobyl accident, such as the enormous increase in childhood thyroid diseases, has made it necessary to establish a new type of medical institution geared not only toward general services but also toward the direct benefits of consultation, medical diagnosis and treatment for the radiation-exposed victims. In the Gomel region of Belarus, the medical examination of the victims has been carried out by the Gomel Regional Specialized Dispensary, which started its work on 10 September 1990 in accordance with decision No. 3358, which was issued effective on 6 September 1990 by the Regional Soviet Deputy Minister of Health.

Mobile teams for outpatient screening have been working at the Dispensary since 1991, their establishment closely linked to the previous humanitarian aid project of "Chernobyl-Sasakawa." At present, there are five mobile teams. The main task of the mobile teams is to perform medical screening of the affected population in the Gomel region. Standard medical screening includes examination by a pediatrician (therapeutist), ultrasound examination of the thyroid gland and general blood analysis. When thyroid and hematological abnormalities are found, patients are introduced to the Polyclinic Department of the Gomel Regional Specialized Dispensary to verify the diagnosis and to provide consultations regarding diagnosis and treatment. The data from these patients are stored in the database of the Gomel Regional Specialized Dispensary, facilitating the process of ongoing observation and treatment. Here, we will introduce our activities at Gomel

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PII: S0531-5131(01)00594-5

Regional Specialized Dispensary and summarize the second Chernobyl-Sasakawa Project conducted from 1997 to 2000.

2. Overall activities

In accordance with an order from the Public Health Ministry dated 4 October 1989, the Gomel Regional Specialized Dispensary adopted another function as a "Regional Radiation Medicine Center." The organization of the Gomel Regional Specialized Dispensary is shown in Fig. 1. The activities of the dispensary include the following.

(1) Medical screening of affected people (adults and children) to identify the groups in need of various types of medical assistance. Patients with thyroid and hematological disorders are referred to the Polyclinic Department of the Gomel Regional Specialized Dispensary to receive consultation, accurate diagnosis and proper treatment. Patients with other physical diseases are referred to other institutions at different levels: district, regional or republic medical institutions.

(2) Extensive examination by the Polyclinic Department and follow-up of persons classified into the second and third groups of primary registration. All of the patients are evaluated for health status, receive a verification of clinical diagnosis, and are referred to specialized regional or republic medical institutions according to the type of the disease.

(3) Treatment and follow-up of outpatients for endocrinological and hematological diseases.

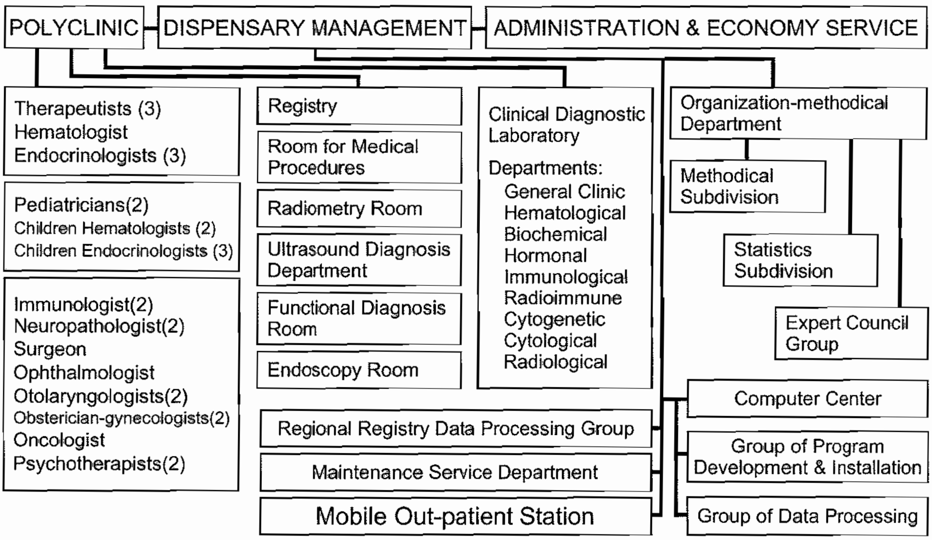

Fig. 1. Organization of the Gomel Regional Specialized Dispensary. The number of doctors exceeding one is indicated by parentheses.

Table 1
Activities of the Gomel Regional Specialized Dispensary in thyroid screening from 1998 to 2000

	Year of examination			Total
	1998	1999	2000	
Screening	53 096	56 130	58 333	167 559
Chernobyl-Sasakawa Project	19 101	21 336	19 488	67 247
Others	33 995	34 794	38 845	100 312
Ultrasound investigations	67 904	70 756	62 125	200 785
Hormonal investigations[a]	75 070	84 038	82 395	241 503
Fine-needle aspiration biopsy	939	1489	1735	4163

[a] Each figure presents the number of investigations.

At present, unfortunately, we have no special facilities for the hospitalization of radiation-exposed victims. There are, however, medical institutions which coordinate specific tasks associated with the mitigation of the medical consequences of the accident: (1) regional department of the state registry which collects medical and dosimetry data on the affected population; and (2) regional expert council which investigates the causality of diseases and mortality.

3. Results

The activities of the Gomel Regional Specialized Dispensary in thyroid screening from 1998 to 2000 are summarized in Table 1, including the second Chernobyl-Sasakawa Project and other projects. About 60 000 patients were examined each year and approximately 80 000 hormone measurements were carried out. About 40% of the investigations have been conducted with the financial support of the Sasakawa Memorial Health Foundation. The thyroid diseases diagnosed in 167 559 people are presented in Table 2. About 5% of the patients with thyroid nodular disorders were found to have thyroid cancer.

A total of 437 thyroid cancers were diagnosed among children and adolescents in Gomel region from 1992 to 2000 and 137 (30%) of these were detected by Gomel Regional Specialized Dispensary (Fig. 2). Continuation of early detection of thyroid diseases in chidlren and adolescents is urgently needed because, as shown in Fig. 2, no significant decrease has been observed in thyroid cancer among children and adolescents. Fig. 3 shows the contribution of the Chernobyl-Sasakawa Project in the diagnosis of

Table 2
Number of patients diagnosed with thyroid diseases for the first time by Gomel Regional Specialized Dispensary

Diagnosis	Year of examination			Total
	1998	1999	2000	
Cancer	33	47	44	124
Nodular goiter	861	885	742	2488
Thyroiditis	402	307	351	1060

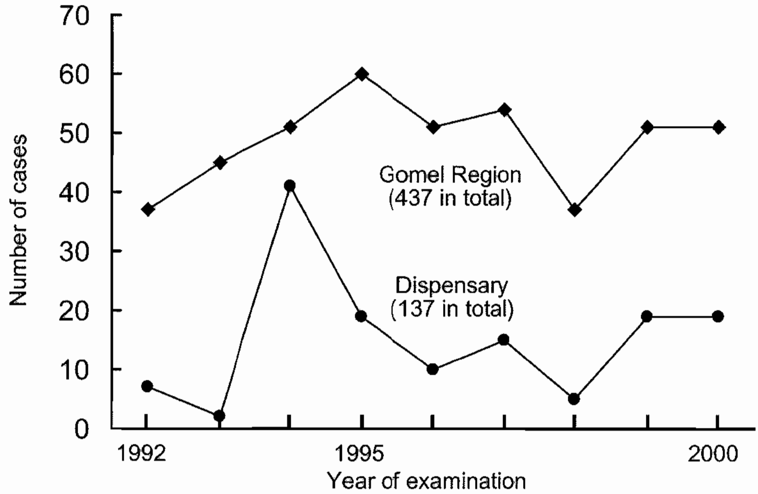

Fig. 2. Annual number of thyroid cancers found in the Gomel region and those detected by the Gomel Regional Specialized Dispensary from 1992 to 2000.

thyroid cancer among children and adolescents in the two periods 1992–1996 and 1998–2000. During the entire period, the Chernobyl-Sasakawa Project discovered 60 (15.7%) out of 437 thyroid cancers. We note that more than one-third of thyroid cancers found in

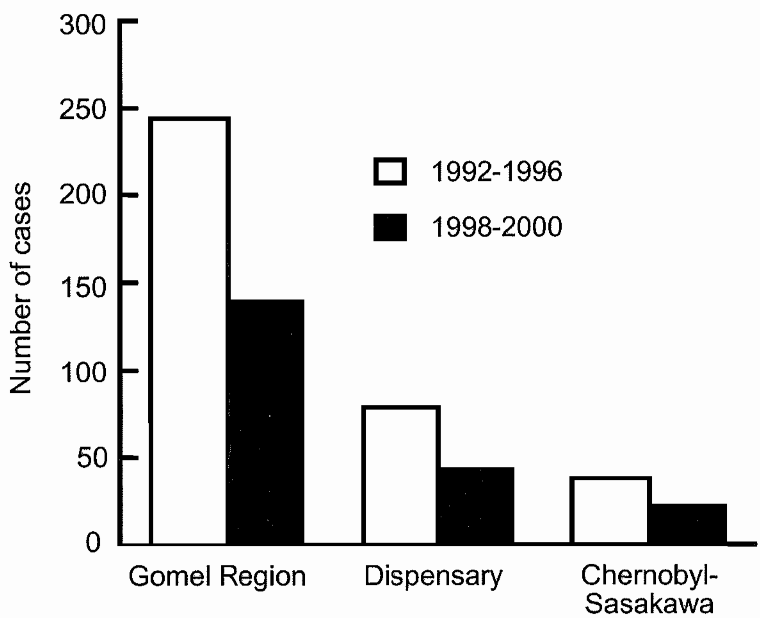

Fig. 3. Contributions of the Gomel Regional Specialized Dispensary and the Chernobyl-Sasakawa Project in the detection of thyroid cancers among children and adolescents in the Gomel region.

Gomel region were diagnosed by Gomel Regional Specialized Dispensary owing to the implementation of the Chernobyl-Sasakawa Project.

From 1998 to 2000, the second stage of the Chernobyl-Sasakawa Project was newly implemented and it included the following three main projects.

(1) A comparative study of more than 38 000 children and adolescents born before and after the Chernobyl accident. In effect, all of the children attending secondary schools in the four agricultural districts of Gomel region and seven secondary schools in Gomel city underwent complete thyroid examination conducted by two mobile teams of the Gomel Regional Specialized Dispensary. As a result, 223 patients with thyroid nodular lesions and 155 patients with autoimmune thyroiditis were found and received follow-up examinations at Gomel Regional Specialized Dispensary. Twenty-two patients with thyroid cancer were referred for surgical treatment in Minsk.

(2) Participation in the case-control project was under the joint collaboration of the Sasakawa Memorial Health Foundation, the Belarussian Center of Medical Technologies and the International Agency for Research on Cancer. Medical supervision of the project was provided in Gomel city and the Gomel region. Out of 1500 targeted subjects, 1200 were examined and the analysis of collected data is under progress.

(3) Regular follow-up of patients with thyroid disorders. All patients with initial diagnoses of thyroid nodular goiter, autoimmune thyroiditis and thyroid cancer regularly receive follow-up examinations by pediatric endocrinologists. Technical support is provided by the "Telemedicine" system in service between Gomel Regional Specialized Dispensary and Nagasaki University since February 1999. The system will make it possible to expand the range of communication to the leading medical institutions in Belarus and abroad. A total of 475 patients including 51 thyroid cancer cases received the advice of Japanese experts, and their regular follow-up examination and treatment are conducted at Gomel Regional Specialized Dispensary.

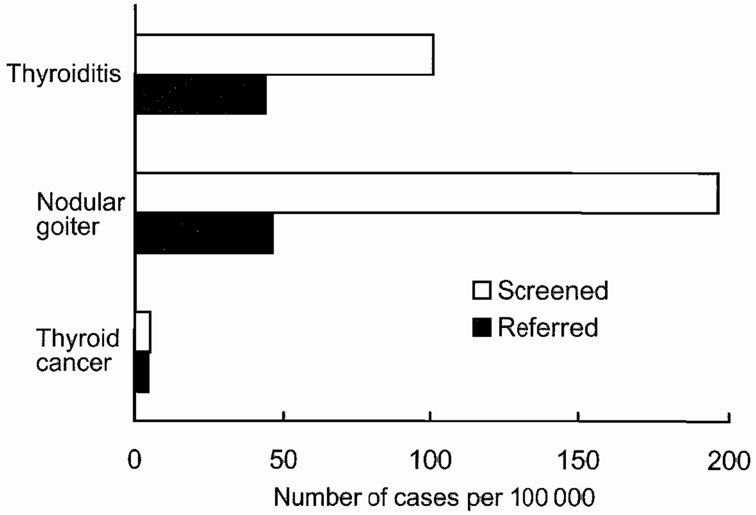

Fig. 4. Prevalence of thyroid diseases among children by type of examination in 2000.

To summarize our activities over the past decade, the Gomel Regional Specialized Dispensary has developed into the leading institution on problems of radiation medicine in the Gomel region, owing to the support of the Sasakawa Memorial Health Foundation and Japanese experts. In particular, the following factors contribute significantly to the increased efficiency of the diagnostic activities.

(1) Development of a mobile form of outpatient examination geared to thyroid screening and the creation of mobile outpatient stations as a powerful independent department.

(2) Methodological approaches in early diagnosis of thyroid diseases based on the consecutive stages of diagnostics: screening with appropriate medical instruments, additional investigations for those whose diagnosis needs confirmation by Polyclinic Department of the Gomel Regional Specialized Dispensary following modern diagnostic procedures such as echo-guided fine-needle aspiration biopsy and cytological analysis.

(3) Use of the "Telemedicine" system for differential diagnostics of thyroid disease in the screened population.

(4) Training courses for our mobile team specialists at Nagasaki University.

Having summarized the data on initial incidence of thyroid diseases in the affected population of the State Registry, we attempted to estimate the efficiency of the screening conducted by our mobile teams.

Figs. 4 and 5 present the prevalence of thyroid abnormalities including thyroid cancer in children and adults in 2000. The prevalence was 1.5–5 times higher in the screened population than in the referred population.

A higher prevalence of thyroid diseases in the screened population can be explained to some extent by over-diagnosis (false-positive diagnosis). However, the comparison of initial data with the findings of verification examinations at the Polyclinic Department of the Gomel Regional Specialized Dispensary demonstrated that at least 75% of cases with

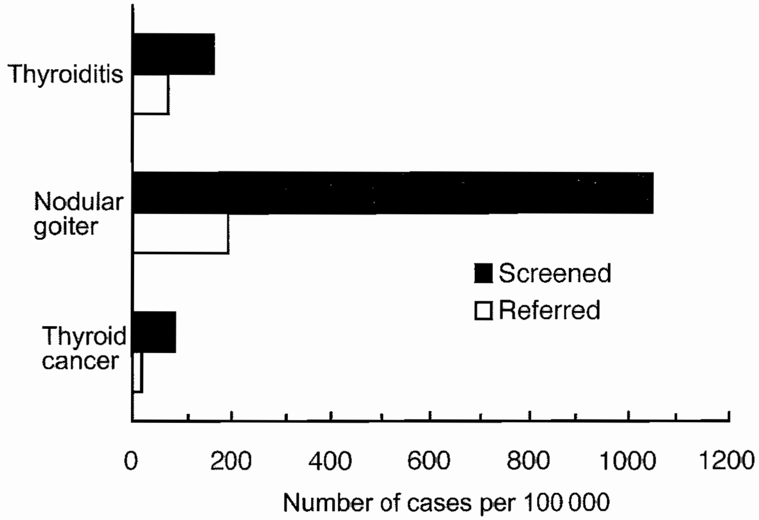

Fig. 5. Prevalence of thyroid diseases among adolescents and adults by type of examination in 2000.

thyroid abnormalities detected by screening was confirmed as abnormal by extensive examinations. We may, therefore, conclude that the Chernobyl-Sasakawa Project findings demonstrate the valid prevalence of thyroid diseases among children and adolescents in the Gomel region. These people are also suffering from iodine deficiency, which may influence the nature of the Chernobyl-induced thyroid diseases. The findings of the examinations from 1997 to 2000 show no decreasing trend in the occurrence of new cases of thyroid cancer. All of these facts make it necessary to extend or, at least, to maintain the current level of medical screening of the targeted population in the Gomel region.

Before concluding the discussion, we would like to mention the future scope and structure of the Gomel Regional Specialized Dispensary. A new dispensary on radiation medicine problems has been under construction since 1993. It is designed to accommodate 500 outpatients and 450 patients, and to have all the departments necessary for children and adults as well as a sanatorium for special diseases (60 beds). The new dispensary will have a department for stem cell transfusion (10 beds), rehabilitation and intensive therapy department (15 beds) and a surgical department with four operating rooms. The total area is 46 802 m^2 and the estimated cost of construction is US$ 78 600 000. Despite the present difficult economic situation in Belarus, we hope that the construction of the Polyclinic Department in the new dispensary will be completed by the beginning of 2002. In this connection, our ongoing joint work with the Sasakawa Memorial Health Foundation is of great importance. We plan to have two specific departments, Hematology and Endocrinology, which will be chaired by the Gomel State Medical Institute. Our foremost desire is continuous cooperation with Sasakawa Memorial Health Foundation and the scientists from Nagasaki University.

4. Conclusions

(1) Screening of the radiation-exposed population reached a high level of efficiency during the period of the Chernobyl-Sasakawa International Medical Cooperation Project.

(2) Approximately 16% of thyroid cancer cases among children and adolescents of the Gomel region were diagnosed owing to the sophisticated assistance of Chernobyl-Sasakawa Project.

(3) Completion of the Gomel Regional Dispensary on the Problems of Radiation Medicine will open new perspectives for international scientific cooperation in the study of health effects of low-dose radiation.

International Congress Series 1234 (2002) 57–65

Thyroid diseases among children and adolescents in Kiev region 15 years after the Chernobyl accident

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Keywords: Thyroid diseases; Kiev; Chernobyl

1. Introduction

Fifteen years have elapsed since the Chernobyl disaster, but at the present time, and in the coming years, the study of radiation effects on the thyroid gland will continue to be a vital undertaking for the mitigation of the consequences of the accident. It is especially important to clarify the other etiological factors of non-radiation origin and to determine the appropriate prophylaxis of thyroid diseases.

A total of about 30 000 children were examined by the "Sasakawa-Chernobyl" Diagnostic Center as part of the Chernobyl Sasakawa Health and Medical Cooperation Project, a 5-year health screening project that began in May 1991 and reached completion at the end of April 1996. From mid-1996 up to the present time, the "Sasakawa-Chernobyl" Diagnostic Center has functioned as a part of Kiev Regional Hospital No. 2 and engaged in the examination of the adult population from the affected areas. The people who were exposed to the accident in childhood are at highest risk because the developing organism is several times more sensitive to radiation than the adult. However, the number of children and adolescents examined over the past 5 years was relatively small because the "Sasakawa-Chernobyl" Diagnostic Center has not received any concrete material support since the conclusion of the above-mentioned project. Furthermore, the examination program was reduced and the majority of children and adolescents examined were those who presented themselves for examination.

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PII: S0531-5131(01)00595-7

2. Subjects and methods

The subjects were 11 086 children and adolescents in the Kiev region examined by the "Sasakawa-Chernobyl" Diagnostic Center of the Kiev Regional Hospital No. 2 from May 1996 to December 2000. Only 1776 (16%) of the subjects underwent health screening by the mobile team of the "Sasakawa-Chernobyl" Diagnostic Center; the remaining 9310 (84%) were referred to us for examination. The age distribution of the subjects is shown in Table 1.

The method of examination was similar to that of the health screening conducted by the Chernobyl Sasakawa Health and Medical Cooperation Project, and the data were stored in the database used in the project [1]. However, measurement of serum free thyroxine (FT_4) and thyroid stimulating hormone (TSH) levels, and titers of anti-thyroglobulin (ATG) antibody and anti-microsome (AMC) antibody were conducted only in cases in which thyroid disease was suspected.

3. Results

A high frequency of diffuse goiter and iodine deficiency was a characteristic feature of the Kiev region among the five regions where the 5-year health screening was conducted in the Chernobyl Sasakawa Health and Medical Cooperation Project [2].

Out of 10 361 children and adolescents (4692 males and 5669 females), diffuse goiter was diagnosed in 4139 (1781 males and 2358 females) (39.9%). The prevalence of diffuse goiter was significantly ($p<0.001$) higher in females than in males, and it showed a significant ($p<0.001$) increase with age in both males and females as shown in Fig. 1.

The urinary iodine concentration was less than 10 μg/dl in 744 (47.7%) of the 1560 children and adolescents measured. The distribution of urinary iodine concentration by district is shown in Fig. 2. A significant correlation was observed (Spearman rank correlation coefficient = 0.65, $p<0.05$) between the prevalence of goiter and iodine deficiency as shown in Fig. 3.

Ultrasonographic thyroid abnormalities were revealed in 1177 (308 males and 869 females) (11.3%) of 10 447 children and adolescents (4727 males and 5720 females). The

Table 1
Distribution of age (years) at the time of examination in study subjects

Group	Male		Female		Total	
	Number of subjects	Age distribution	Number of subjects	Age distribution	Number of subjects	Age distribution
Referred	4170	(10, 12, 14)[a] 4–19[b]	5140	(10, 12, 14) 4–19	9310	(10, 12, 14) 4–19
Screened	695	(10, 12, 14) 4–19	1081	(11, 13, 14) 4–17	1776	(10, 12, 14) 4–19
Total	4865	(10, 12, 14) 4–19	6221	(10, 12, 14) 4–19	11 086	(10, 12, 14) 4–19

[a] Each triplet gives the 25th, 50th and 75th sample percentiles of age distribution at the time of examination.
[b] Minimum and maximum.

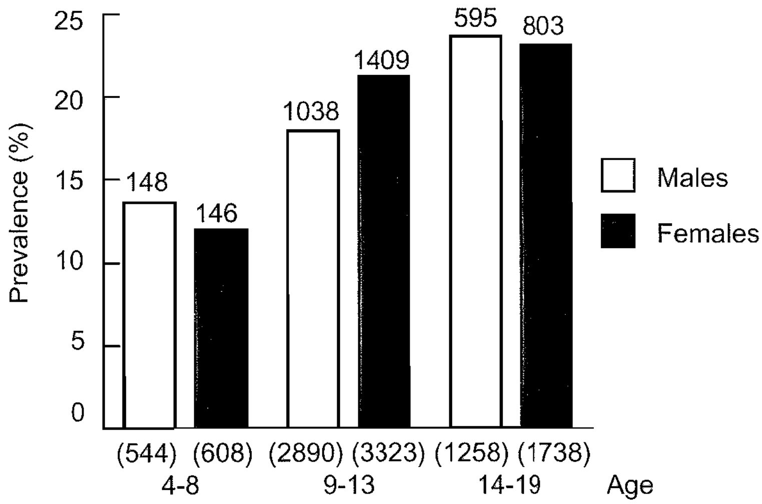

Fig. 1. Prevalence of diffuse goiter by sex and age among children and adolescents in Kiev region who were examined by the "Sasakawa-Chernobyl" Diagnostic Center from May 1996 to December 2000. The figure in parentheses and the figure on the bar denote the number of subjects examined and number of cases, respectively.

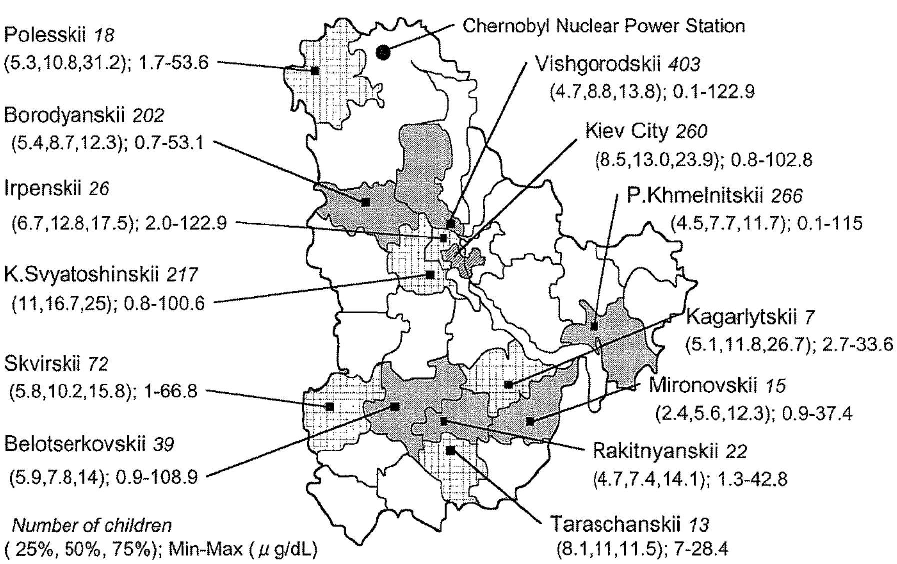

Fig. 2. Distribution of urinary iodine concentration (μg/dl) by district in Kiev region. Italics denote the number of subjects who underwent measurements of urinary iodine concentration. The triplets give the 25th, 50th and 75th sample percentiles of the measurements, and the two figures following the triplets denote the minimum and maximum of the measurements.

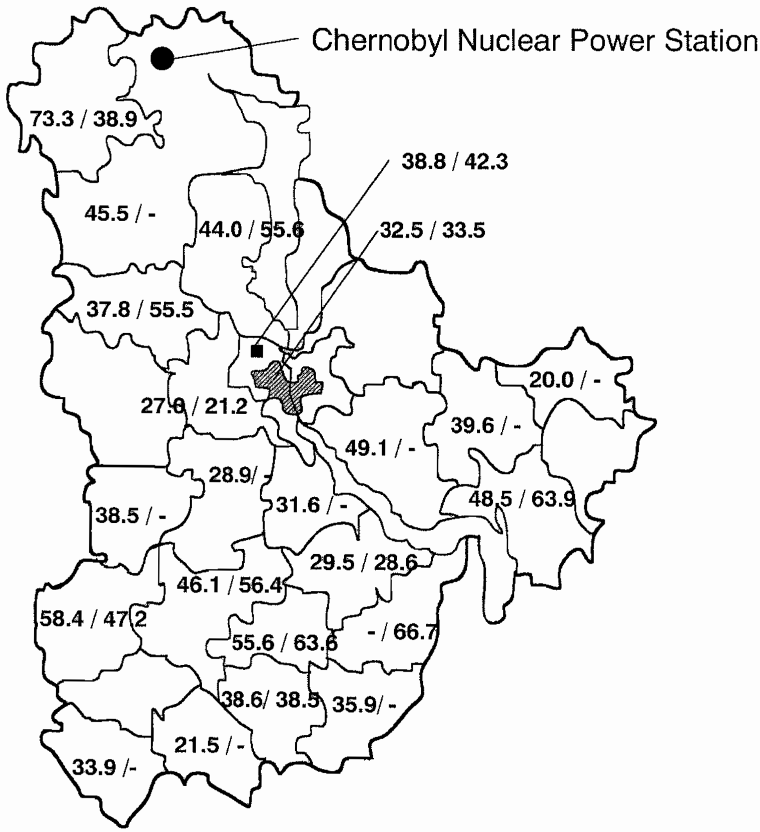

Fig. 3. The prevalence of diffuse goiter and iodine deficiency by district in Kiev region. The figures on the left and right of the slash denote the prevalence of diffuse goiter and iodine deficiency in percentage, respectively. The minus mark indicates that data were unavailable.

prevalence of ultrasonographic thyroid abnormalities was significantly ($p<0.001$) higher in females than in males and showed a significant ($p<0.001$) increase with age in both males and females as shown in Fig. 4. Nodular goiter was diagnosed in 60 (14 males and 46 females) (0.6%) of 10 845 children and adolescents (4800 males and 6045 females). The prevalence of nodular goiter was significantly ($p<0.01$) higher in females than in males and showed a significant ($p<0.01$) increase with age in both males and females as shown in Fig. 5. Thyroid cystic lesions were found in 69 (14 males and 46 females) (0.6%) of 10 835 children and adolescents (4799 males and 6036 females). The prevalence of thyroid cystic lesions was significantly ($p<0.001$) higher in females than in males and showed a significant ($p<0.001$) increase with age in both males and females as shown in Fig. 6.

Out of 5107 children and adolescents (2033 males and 3074 females) who underwent measurement of titers of ATG antibodies, 250 (44 males and 206 females) (4.9%) had positive ATG antibodies. The prevalence of positive ATG antibodies was significantly

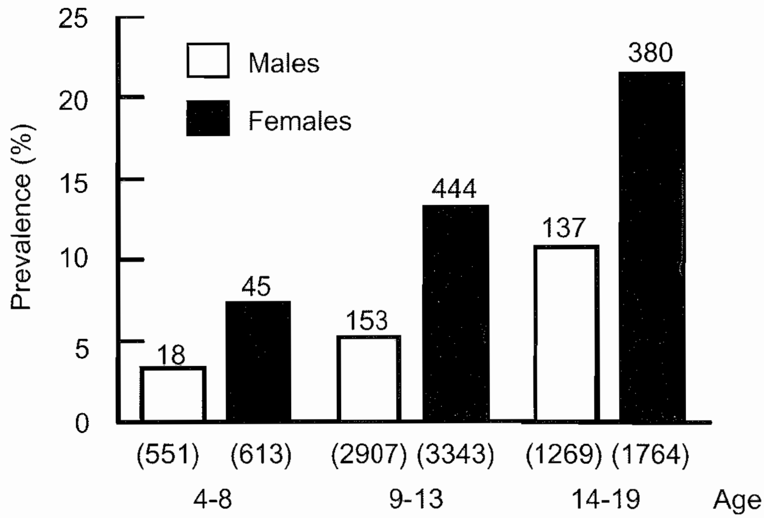

Fig. 4. Prevalence of ultrasonographic thyroid abnormalities by sex and age among children and adolescents in Kiev region who were examined by the "Sasakawa-Chernobyl" Diagnostic Center from May 1996 to December 2000. The figure in parentheses and the figure on the bar denote the number of subjects examined and number of cases, respectively.

($p<0.001$) higher in females than in males and showed a significant ($p<0.05$) increase with age in females, while in males no significant association was observed between the prevalence of positive ATG antibodies and age (Fig. 7). Similarly, out of 5106 children and

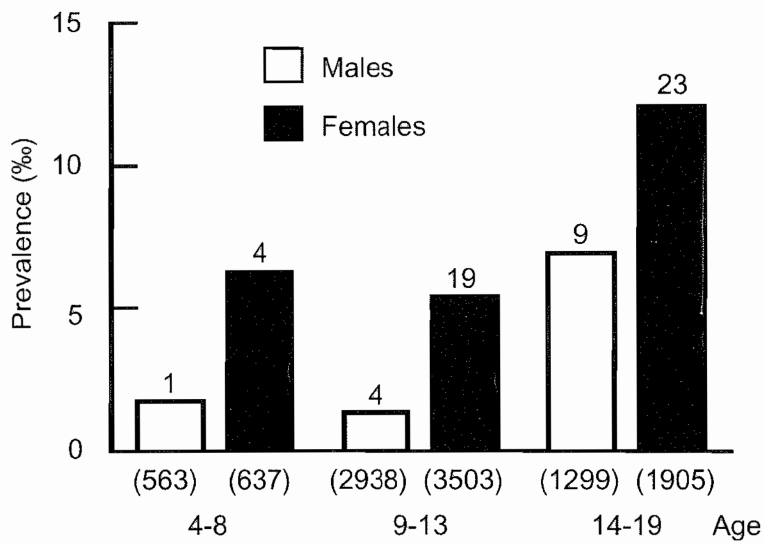

Fig. 5. Prevalence of nodular goiter by sex and age among children and adolescents in Kiev region who were examined by the "Sasakawa-Chernobyl" Diagnostic Center from May 1996 to December 2000. The figure in parentheses and the figure on the bar denote the number of subjects examined and number of cases, respectively.

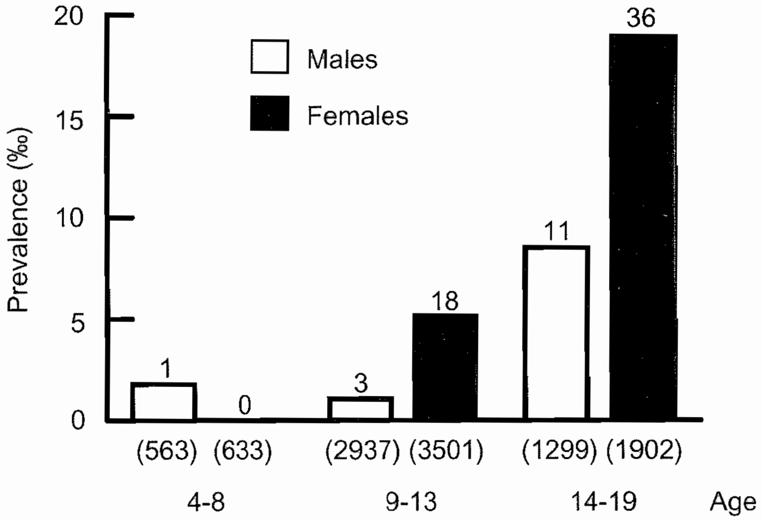

Fig. 6. Prevalence of thyroid cystic lesions by sex and age among children and adolescents in Kiev region who were examined by the "Sasakawa-Chernobyl" Diagnostic Center from May 1996 to December 2000. The figure in parentheses and the figure on the bar denote the number of subjects examined and number of cases, respectively.

adolescents (2034 males and 3072 females) who underwent measurement of titers of AMC antibodies, 447 (77 males and 370 females) had positive AMC antibodies. The prevalence of positive AMC antibodies was significantly (p<0.001) higher in females than in males

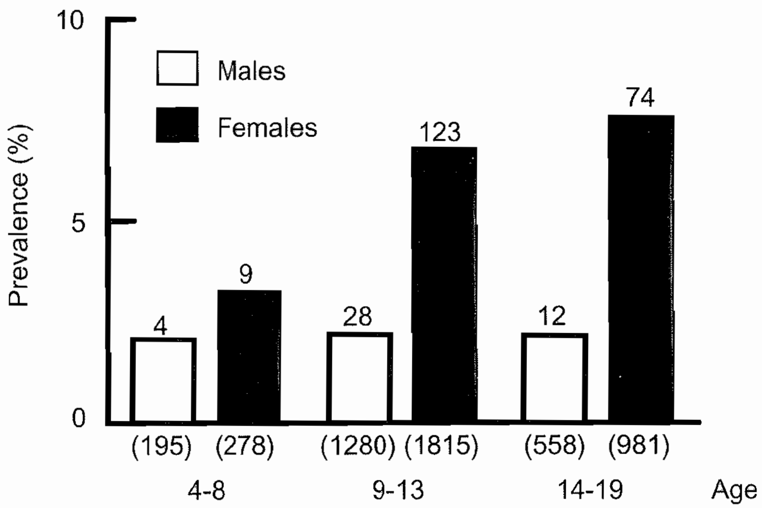

Fig. 7. Prevalence of positive ATG antibodies by sex and age among children and adolescents in Kiev region who were examined by the "Sasakawa-Chernobyl" Diagnostic Center from May 1996 to December 2000. The figure in parentheses and the figure on the bar denote the number of subjects who were measured titers of ATG antibodies and number of subjects with positive ATG antibodies, respectively.

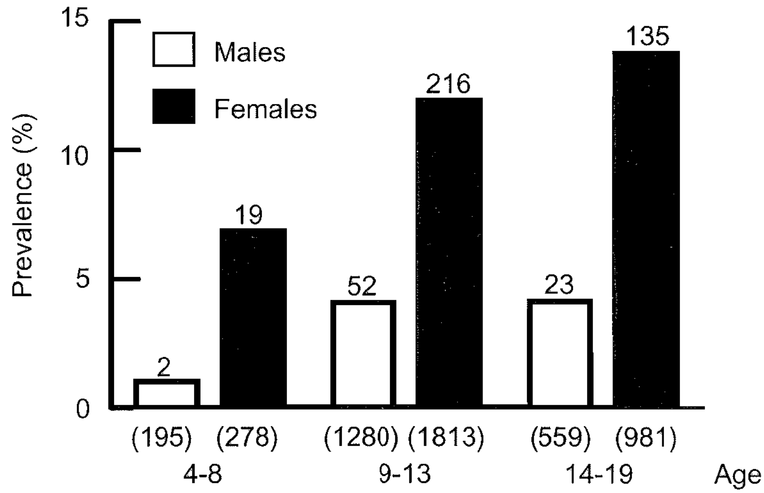

Fig. 8. Prevalence of positive AMC antibodies by sex and age among children and adolescents in Kiev region who were examined by the "Sasakawa-Chernobyl" Diagnostic Center from May 1996 to December 2000. The figure in parentheses and the figure on the bar denote the number of subjects who were measured titers of AMC antibodies and number of subjects with positive AMC antibodies, respectively.

and showed a significant ($p<0.01$) increase with age in females, while in males no significant association was observed between the prevalence of positive AMC antibodies and age (Fig. 8).

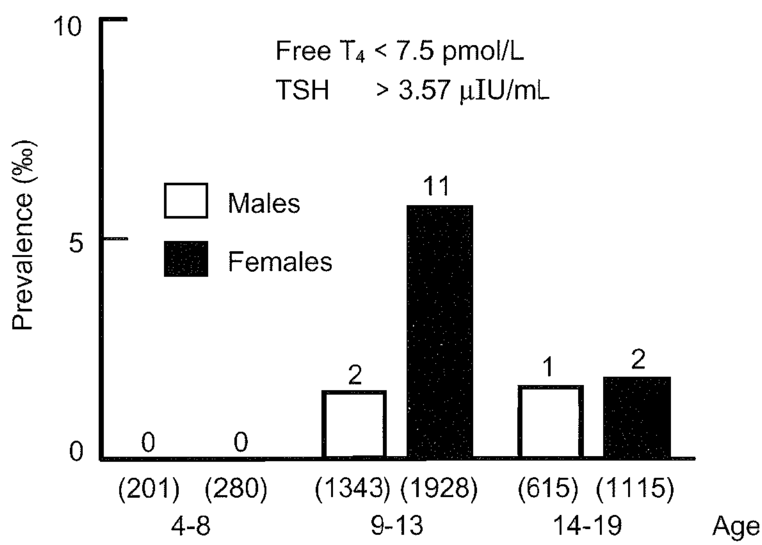

Fig. 9. Prevalence of hypothyroidism by sex and age among children and adolescents in Kiev region who were examined by the "Sasakawa-Chernobyl" Diagnostic Center from May 1996 to December 2000. The figure in parentheses and the figure on the bar denote the number of subjects examined and number of cases, respectively. Hypothyroidism was diagnosed when $FT_4<7.5$ pmol/l and TSH >3.57 μIU/ml.

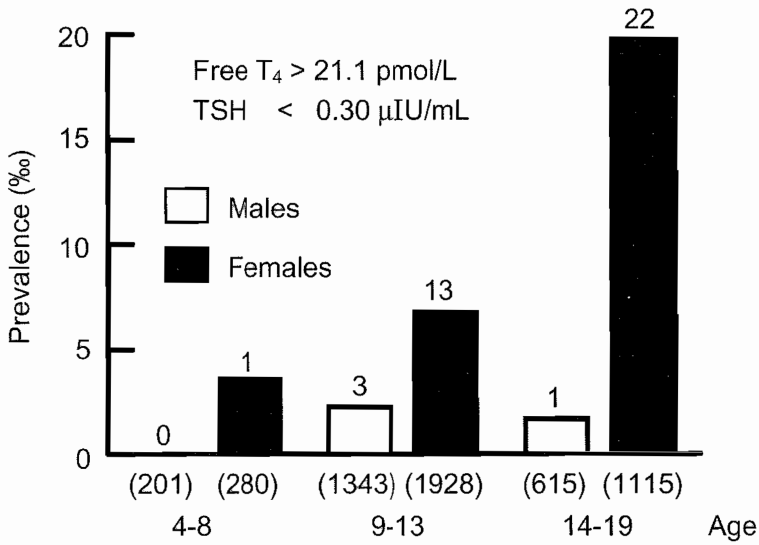

Fig. 10. Prevalence of hyperthyroidism by sex and age among children and adolescents in Kiev region who were examined by the "Sasakawa-Chernobyl" Diagnostic Center from May 1996 to December 2000. The figure in parentheses and the figure on the bar denote the number of subjects examined and number of cases, respectively. Hyperthyroidism was diagnosed when $FT_4 > 21.1$ pmol/l and TSH < 0.30 μIU/ml.

Out of 5482 children and adolescents (2159 males and 3323 females) who underwent measurement of TSH and FT_4 levels, hypothyroidism and hyperthyroidism were diagnosed in 16 (3 males and 13 females) and 40 (4 males and 36 females), respectively. No

Table 2
Thyroid cancers revealed by fine-needle aspiration biopsy at Kiev Regional Hospital No. 2 among 2012 patients with nodular and cystic lesions in the period from 1996 to 2001

Age at the time of the Chernobyl accident (years)	Sex[a]	Age at examination (years)					Total
		10–19	20–29	30–39	40–49	50–	
0–9	M	6	1				7
	F	7	2				9
10–19	M		1				1
	F		5	3			8
20–29	M			2	2		4
	F			16	9		25
30–39	M				4	5	9
	F				18	9	27
40–49	M					7	7
	F					13	13
50–	M					6	6
	F					8	8
Total	M	6	2	2	6	18	34
	F	7	7	19	27	30	90

[a] M = male, F = female.

significant difference was observed between males and females in the prevalence of hypothyroidism (Fig. 9). On the other hand, the prevalence of hyperthyroidism was significantly ($p<0.01$) higher in females than in males and showed a significant ($p<0.01$) increase with age in females, although no association with age was observed in males (Fig. 10).

Fine-needle aspiration biopsy was performed at Kiev Regional Hospital No. 2 on 2012 patients with nodular and cystic lesions in the period from 1996 to 2001, and thyroid cancer was found in 124 (34 males and 90 females) (6.2%) of these patients. Table 2 classifies the cancer cases by age at the time of the Chernobyl accident, sex and age at examination. Sixteen of the cancer cases (7 males and 9 females) were under 10 years of age, and 13 (6 males and 7 females) were diagnosed in childhood or adolescence.

4. Conclusions

The present study on children aged 0–10 years at the time of the Chernobyl accident indicated a continuous increase in the risk of developing thyroid diseases. Thyroid abnormalities were observed more frequently in females than in males. Although iodine deficiency induces an increase in thyroid abnormalities, it is not the unique cause of thyroid abnormalities.

The results of the present study have important implications for the detection of abnormalities, treatment of children at an early stage of thyroid disease, and follow-up treatment.

References

[1] Y. Shibata, S. Yamashita, M. Hoshi, K. Fujimura, Chernobyl Sasakawa Health and Medical Cooperation Project: materials and methods, in: S. Yamashita, Y. Shibata (Eds.), Chernobyl: A Decade, Elsevier, Amsterdam, 1997, pp. 23–38.

[2] N.V. Nikiforova, A.V. Nedozhdy, S.V. Semushina, et al., Findings of the Chernobyl Sasakawa Health and Medical Cooperation Project: goiter and iodine around Chernobyl, in: S. Yamashita, Y. Shibata (Eds.), Chernobyl: A Decade, Elsevier, Amsterdam, 1997, pp. 85–92.

Overview of thyroid diseases around Chernobyl

International Congress Series 1234 (2002) 69–75

Thyroid cancer in Belarus

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Abstract

The Chernobyl accident in April and May of 1986 promoted thyroid carcinomas in 1500 patients who were exposed to radiation at the age group under 18. The common type of malignancy was papillary cancer (93.5%). For the period from 1990 to 2000, thyroid carcinomas were diagnosed in 674 children (age group under 15), in 262 adolescents (age group between 15 and 19) and in 564 young adults (age group from 19 to 33). The highest number of thyroid malignancies in children and adolescents was diagnosed in Gomel and Brest oblasts located closer to the Chernobyl Nuclear Power Plant. For 15 years (1986–2000), spontaneous (non-radiogenic) thyroid carcinomas appeared only in 17 children. Thyroid cancer promoted by radiation in children possesses the behavior to form the regional (73%) and distant (16.6%) metastases, mainly in lung. As a result of performed risk analysis for the cohort exposed at the age group under 18, the following values were obtained: 1.93 (1.79–2.06) per 104 PYGy for the absolute risk coefficient, and 37.66 (35.06–40.26) per Gy for the excess relative risk coefficient.

Keywords: Thyroid cancer; Estimated risk; Chernobyl accident; Incidence

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0531-5131/02
PII: S0531-5131(01)00596-9

1. Introduction

The Chernobyl accident greatly affected thyroid cancer incidence rate in Belarus [1]. It was for the first time that the patients with thyroid cancer induced by radiation appeared on the territory of the republic [2]. This resulted in considerable incidence growth of differentiated forms of tumors, mostly of papillary cancer, in people of all ages in all the six regions of Belarus [3–5]. After Chernobyl, thyroid cancer in children appeared to become the most frequent oncological pediatric disease [6].

2. Materials and methods

The research is conducted on materials of the Thyroid Cancer Center. The therapeutic and follow-up data were analysed. The materials of the National Cancer Registry were used also. The cases of thyroid cancer proved in 1990–2000 years are included in the analysis.

An assessment of thyroid cancer risk considering gender difference was performed for the cohort of people exposed in the 0–18-year-old age group. Thyroid dose reconstruction was performed using radioecological model elaborated to include specific for Belarus parameters. Demographic data was calculated based on Census data for 1989 using methods of age–gender pyramids, correction of absolute age structure and back movement of age groups [7,8].

3. Results and discussion

After Chernobyl, in comparison with pre-accident period, the thyroid cancer incidence increased in children by 88.5 times, in adolescents—by 11.8 times, in adults—by 4.6 times (Table 1).

From 1990 to 2000, thyroid cancer was detected in 6905 patients, including 691 children (among them 674 were born before the accident), 262 adolescents and 5952 adults (Table 2).

Predominantly there was papillary thyroid cancer (Table 3).

The highest amount of cancer cases has been registered in Gomel region. Children and adolescents have compounded 29.8% (Table 4).

Table 1
Thyroid cancer in Belarus before and after the Chernobyl accident

Patients' age	1971–1985	1986–2000	Total
0–14	8	703	711
15–18	21	267	288
19+	1465	6719	8184
Total	1494	7689	9183

Table 2
Age of thyroid cancer patients at the time of diagnosis; cases revealed in 1990–2000

Gender	Number of patients	Age (years)				
		0–4	5–9	10–14	15–18	19+
Male	1328	1	62	199	94	972
Female	5577	5	105	319	168	4980
Both genders	6905	6	167	518	262	5952
%	100	0.1	2.4	7.5	3.8	86.2

Table 3
Histological type of thyroid cancer

Histological type of thyroid cancer	Number of cases	Age at the time of cancer detection (years)					
		0–14		15–18		19+	
		n	%	*n*	%	*n*	%
Papillary	5998	651	94.2	245	93.5	5102	85.7
Follicular	580	35	5.1	14	5.3	531	8.9
Medullary	127	4	0.6	3	1.2	120	2.0
Undifferentiated	168	1	0.1	0	0	167	2.8
Squamous	32	0	0	0	0	32	0.6
Total	6905	691	100	262	100	5952	100

Cancer in children and adolescents was diagnosed nearly throughout the territory of Belarus, but predominantly in the Gomel and Brest regions (Fig. 1).

The dramatic growth of pediatric cancer patients began in 1990 (in 4 years after the Chernobyl accident) [1,2], has lasted for 6 years and reached its peak—90 cases—in 1995 [6]. The years that followed were characterized by a gradual decrease of cancer incidence in children and the increase of it in adolescents (Fig. 2).

In 2000, the incidence rate per 100 000 children, adolescents and adults of the Gomel region amounted to 5.4, 33.7 and 15.9 cases, respectively (Fig. 3).

The high frequency of thyroid cancer in regions is marked apart, where the radiation dose of the thyroid gland was more than 1 Gy (Fig. 4).

Table 4
Thyroid cancer among population of Belarus by region

Region	Cases	Children and adolescents	
		n	%
Gomel	1693	504	29.8
Minsk-city	1218	70	5.7
Mogilev	1016	55	5.4
Vitebsk	923	14	1.5
Brest	872	219	25.1
Minsk	760	46	6.1
Grodno	423	45	10.6
Belarus	6905	953	13.8

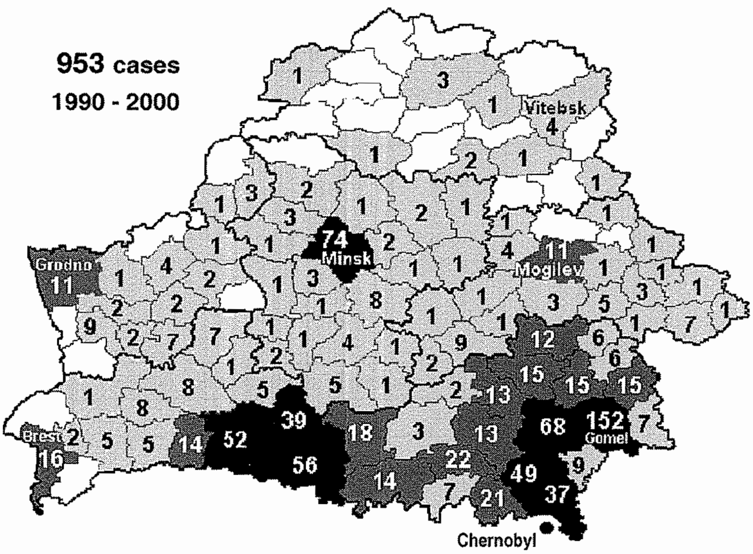

Fig. 1. Distribution of 953 cases of children and adolescent thyroid cancer revealed in 1990–2000 by district of Belarus.

The cohort was divided into the following groups according to the estimated absorbed thyroid dose: 0–0.3; 0.3–0.6; 0.6–1.0; 1.0–2.0; 2 Gy or more. In accordance with the calculated individual doses for persons with the thyroid cancer, the percent distribution of excess thyroid cancer cases for dose intervals was the following: 37.7% thyroid cancer cases among people exposed to doses less than 0.3 Gy, 45.4% to 0.3–1 Gy, and 16.9% to more than 1 Gy.

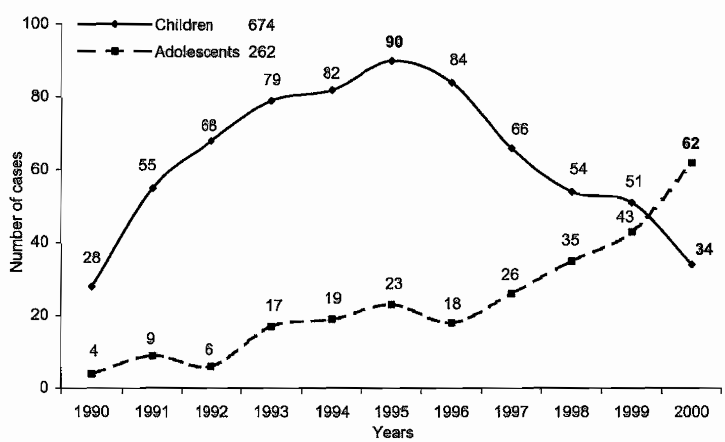

Fig. 2. Annual number of children and adolescent thyroid cancer cases in Belarus.

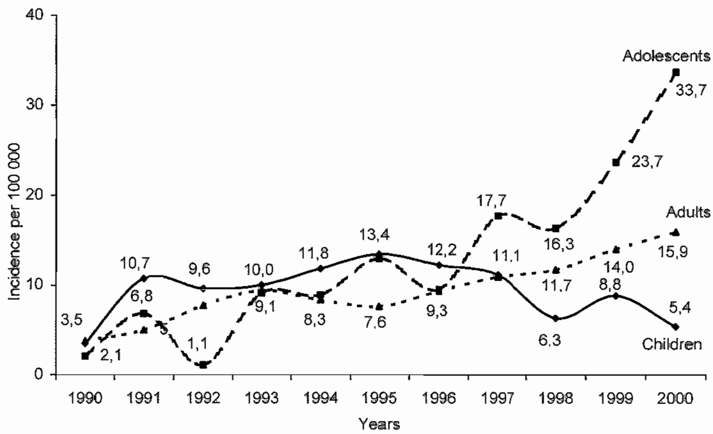

Fig. 3. Annual incidence (per 100 000) of thyroid cancer in Gomel region.

It is known that the level of average dose is higher for those exposed at a younger age. Therefore, cohort of exposed at a younger age had higher collective dose than those exposed at an older age. Consequently, more cases of thyroid cancer were observed among children exposed at a younger age (Fig. 5). Analysis of the correspondence between the number of excess thyroid cancer and the level of collective dose for different age groups showed that for the age group under 11 the number of cases is proportional to the collective dose for boys and girls. For the older cohort (age group between 11 and 18), this proportionality is violated with ratio being higher for girls than for boys.

Radiation induced differentiated thyroid cancer has highly aggressive characteristic features (the lung metastasis in children have arisen in 16.6% of cases).

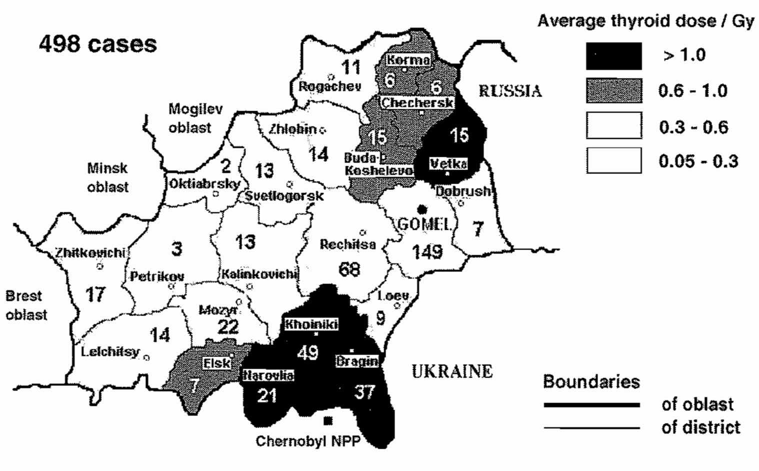

Fig. 4. Distribution of 498 children and adolescent thyroid cancers by district of Gomel region with average thyroid dose.

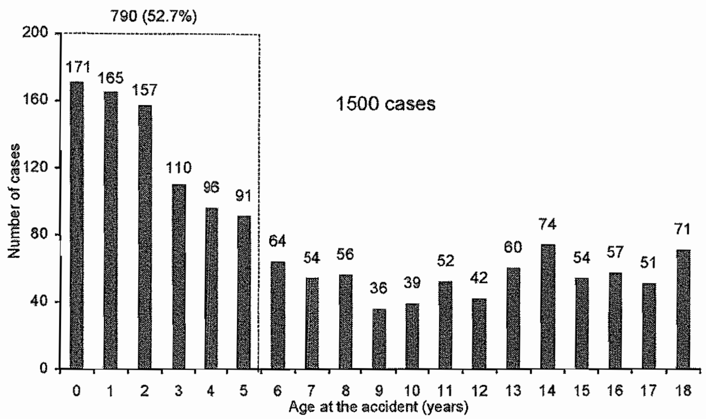

Fig. 5. Number of thyroid cancer cases by age at the accident (0–18 years of age).

From 1500 patients with irradiated thyroid glands during accident, 11 patients (three children, two adolescents and six adults) have died because of distant metastases that has compounded 0.7%.

Even microcarcinoma of 3–9 mm diagnosed in 377 patients (age group from 6 to 33) often resulted in multifocal growth (17.0%), extrathyroid tissue invasion (8.0%), regional metastases (47.2%) and lung metastases (3.7%).

4. Conclusion

Within the period of 30 years (1971–2000), spontaneous thyroid cancer in Belarus occurred in 25 children, 17 of which were born after the accident.

Out of 1635 cases, 691 cases—in children, 262—in adolescents, 564—in young adults (age group from 19 to 33) may be referred to as radiation-induced cancer patients irradiated at the age of 18 including 135 liquidators. The irradiation doses and pathogenetic interconnection with radiation for the rest of the 5270 adult thyroid cancer patients are still to be cleared out.

The Chernobyl tragedy concerning only children is finished. A new period of considerable thyroid cancer incidence growth in young adult population (age group from 15 to 33) has commenced. The aggressive character of pediatric radiation-induced cancer still cannot be explained.

The value of excess absolute risk coefficient calculated for the first nine years period of Plato after the 4-year latent period for the cohort of people exposed at the age group under 18 is 1.93 (1.79–2.06) per 104 PYGy; excess relative risk of 37.66 (35.06–40.26) per Gy. For girls, the absolute risk was calculated as 2.6 (2.4–2.86) per 104 PYGy, for boys—1.3 (1.17–1.5) per 104 PYGy. The ratio between boys and girls for absolute risk coefficient is 1:2 for the total cohort under consideration, however, there is a significant variation for different age groups.

References

[1] V. Kazakov, E. Demidchik, L. Astakova, Thyroid cancer after Chernobyl, Nature 359 (1992) 21–22.
[2] E. Demidchik, I. Drobyshevskaya, E. Cherstvoy, L. Astakhova, A. Okeanov, T. Vorontsova, M. Germenchuk, Thyroid cancer in children in Belarus, The radiological consequences of the Chernobyl accident. Minsk, Belarus, (18–22.03.1996) 677–682.
[3] M. Ito, S. Yamashita, K. Ashizawa, T. Hara, H. Namba, M. Hoshi, Y. Shibata, I. Sekine, L. Kotova, G. Panasyuk, E. Demidchik, S. Nagataki, Histopathological characteristics of childhood thyroid cancer in Gomel, Belarus, Int. J. Cancer 65 (1996) 29–33.
[4] E.P. Demidchik, A.F. Tsyb, E.F. Loushnikov, Thyroid Cancer in Children, Medizina, Moscow, 1996 (in Russian).
[5] E.P. Demidchik, V.S. Kazakov, L.N. Astakhova, A.E. Okeanov, Yu.E. Demidchik, Thyroid cancer in children after the Chernobyl accident: clinical and epidemiological evaluation of 251 cases in the Republic of Belarus, Nagasaki Symposium on Chernobyl: Update and Future, Elsevier, Amsterdam, 1994, pp. 21–30.
[6] E.P. Demidchik, Yu.E. Demidchik, Thyroid cancer promoted by radiation in the children of Belarus, in: 10th International Congress of Radiation Research, Würzburg, Germany, vol. 2 (1995) 1143–1146.
[7] E.P. Demidchik, Y.E. Kenigsberg, E.E. Bouglova, A.L. Golovneva, Thyroid cancer in children and adolescents in Belarus exposed due to the Chernobyl accident: current date and prognosis, Med. Radiol. Radiats. Bezop. 2 (1999) 26–35 (in Russian).
[8] E. Buglova, A. Golovneva, Y. Kenigsberg, J. Kruk, E. Demidchik, Risk analysis for thyroid cancer cases among children and adolescents of Belarus exposed due to the Chernobyl accident. Medical and biological aspects of the Chernobyl accident, Anal. Inf. Bull., Minsk, (2) (2000) 3–12 (in Russian).

International Congress Series 1234 (2002) 77–83

Summary of the 15-year observation of thyroid cancer among Ukrainian children after the Chernobyl accident

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Abstract

According to the data of the clinico-morphological register of the Institute of Endocrinology and Metabolism in Ukraine, for the post-Chernobyl period in Ukraine (1986–2000), 472 cases of thyroid cancer have been reported in children who have been operated at the age of up to 15 years, among which, 431 were born before the Chernobyl accident, 11 were "in utero" at the time of the accident, and 30 were born after the Chernobyl accident. The largest number of cases (57) has been reported in 1996, which made up 0.57 per 100 000 children aged 0–14, and exceeded by 11.4 times the average pre-Chernobyl incidence rate (0.05) in this age group. The highest incidence rate has been reported in six regions of Ukraine which have been the most contaminated by iodine radionuclides (Kiev, Chernigov, Zhitomir, Rovno, Cherkassy regions, and Kiev City). The additional incidence in these regions was rising with increasing thyroid exposure dose, and this is most evident for a dose over 0.5 Gy. Morphological studies showed that in most of cases, the tumors under study (92.1%) represented papillary carcinoma (with a dominant solid–follicular structure) that were characterized by a high incidence of regional metastastic spreading (62% of cases). © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Thyroid cancer; Children; Register; Exposure doses; Pathology

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PII: S0531-5131(01)00597-0

1. Introduction

Numerous investigations which were carried out during the last 15 years have demonstrated that the most urgent problem that arose from the Chernobyl accident is the problem of thyroid pathology, especially thyroid cancer in children [1–10]. This catastrophe differed from those which occurred in world practice until now (atomic bombardment of Hiroshima and Nagasaki, hydrogen bomb test on Marshall Islands), both by the spectrum of radionuclides released to the atmosphere, and by the health aftereffects, in particular, a reliable increase in thyroid cancer reported in the children of Belarus and Ukraine 4 years after the Chernobyl catastrophe [1–5,7–9,11–13].

Since children who have been exposed to radiation following the Chernobyl catastrophe, and in which thyroid cancer has also appeared in childhood (before the age of 15), are no longer registered beginning 2001 (they passed the group of adolescents and young adults), it seems to be of great importance to make a complete analysis of thyroid cancer incidence in this age group for the entire post-Chernobyl period.

2. Materials and methods

The analysis was conducted using the data of a register established at the Institute of Endocrinology and Metabolism of the AMS of Ukraine [7,9]. At present, this register includes 1906 cases of thyroid cancer revealed in Ukraine in patients born in 1968, and later for the period 1986–2000 (data for 2000 is still preliminary). The number of thyroid cancer cases in children having been operated on at the age of up to 15 is equal to 472. The incidence per 100 thousand children aged 0–14 has been calculated, a comparison of the incidence in the six regions of Ukraine being the most contaminated by iodine radionuclides (Kiev, Chernigov, Zhitomir, Rovno, Cherkassy regions, and Kiev City) and the other 21 regions of Ukraine has been made.

To analyse the dose-dependence of thyroid cancer incidence in children, a clusterization has been made of the above regions (Kiev region was considered along with Kiev City) in the areas having the same rate of average thyroid exposure doses (dose zones). In this case, average doses "per capita" for a district for the corresponding age cohort were considered as average ones. For each of the six established dose clusters, a population aged 0–14 years has been estimated in four periods of follow-up: latent period (1986–1989) and three post-latent periods (1990–1992; 1993–1995 and 1996–1998).

To estimate the spontaneous incidence rate of thyroid cancer in the cohort aged 0–14 (at the time of surgery), power function was used, whose parameters were assessed according to the data on thyroid cancer incidence in the whole territory of Ukraine in the latent period. For each of the periods, a spontaneous incidence rate was calculated, taking into account the differences in age composition of the cohort 0–14 years at the moment of surgery in different periods of follow-up. So, if in the latent period (1986–1989) in this age cohort, all age groups were represented (though in different proportions); in 1996–1998, only age cohorts 10–14 years at the moment of surgery were represented.

A pathomorphological analysis was performed on 314 cases of thyroid carcinomas which were removed in children in 1986–2000 at the Department of Surgery of the

Institute of Endocrinology and Metabolism of the AMS of Ukraine, or on material (paraffin blocks, histological specimens) forwarded to the Laboratory of Morphology of the institute for consultative conclusion.

3. Results

In assessing the data of the register concerning the number of thyroid cancer cases in the age group 0–14 years at the time of surgery, it should be noted that for the post-Chernobyl period (1986–2000), 472 cases of the disease have been reported in Ukraine. It should be stressed that while for the pre-Chernobyl period (1981–1985) only 25 cases of cancer have been revealed in children (five cases per year on average), from 1986 to 1990, there were 61 cases (12 per year on average), and in 1991–1995, 220 cases have been reported (44 per year on average). In 1996–2000, 191 cases (38 per year on average) have been registered, a decrease in the number of cases in 1999–2000 as shown in Table 1. It should be noted that out of 472 cases, 431 have been reported in children born before the accident, 11 cases in children born in the first months after the accident (thyroid exposure took place in the last trimesters of pregnancy), and only 30 cases have been revealed in children born after the Chernobyl catastrophe (one in 1991; one in 1992; one in 1993; one in 1994; two in 1995, four in 1996, two in 1997, two in 1998, five in 1999, and eleven in 2000).

The incidence per 100 000 population of children in Ukraine as a whole for the period 1981–1985 varied within the range from 0.04 to 0.06; 0.05 on average. In 1986–1990, this indicator had increased by 2.2 times (0.11), in 1991–1995 by 8 times (0.40), and in 1996–2000 by 8.2 times (0.41) as compared to the average pre-Chernobyl rate. Maximum incidence rates have been reported in 1996 (0.57). In the following years, the incidence was decreasing, most significantly in 1999–2000: up to 0.30 and 0.28 cases per 100 000 children, respectively (Table 1).

The rise in the incidence occurred mainly in the abovementioned regions being the most contaminated by iodine radioisotopes. In these six regions, the average annual incidence in the pre-Chernobyl period was only 0.009 (one case of cancer in a child from Cherkassy region).

In 1986–1990, the incidence rate had increased in the abovementioned regions up to 0.18, which was twice as high as the total rate for the other 21 regions (0.09). In 1991–1995 the incidence was equal to 1.38, being 8.1 times as high as in other regions (0.17). In 1996–2000 the incidence per 100 000 children in the above six regions (1.27) exceeded by 6.7 times the average rate for the rest of the territory of Ukraine (0.19). It should be

Table 1
Number of thyroid cancer cases and incidence per 100000 children (aged 0–14 years at the time of surgery) in Ukraine

	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000
Number of cases	8	7	8	11	27	25	53	47	48	47	57	38	45	27	24
Incidence	0.07	0.06	0.07	0.10	0.24	0.23	0.49	0.44	0.46	0.46	0.57	0.39	0.48	0.30	0.28

Table 2
Incidence of thyroid cancer per 100000 children (aged 0–14 years at the time of surgery) in six of the most contaminated and 21 other regions of Ukraine

	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000
6 Regions	0.13	–	0.09	0.18	0.51	0.66	1.7	1.4	1.4	1.7	1.9	1.5	1.5	1.0	0.46
21 Regions	0.06	0.08	0.07	0.08	0.18	0.12	0.18	0.20	0.22	0.17	0.25	0.13	0.24	0.12	0.23

stressed that in spite of a decrease in the average incidence for Ukraine in 1999–2000, such an excessive rate was preserved in the above six regions versus the rest of the territory, especially in 1999 (Table 2).

Unlike the pattern described, in children born after the Chernobyl catastrophe, the cases of thyroid cancer are more often reported in 21 non-contaminated or less contaminated regions of Ukraine (73% of cases), which is additional evidence of the radiation genesis of thyroid cancer in children having undergone the consequences of the Chernobyl catastrophe.

The analysis of distribution of children with thyroid carcinoma by age at the time of the accident has shown that a maximum number of cases (311 out of 442 or 70.4%) was revealed in children having been exposed at the age of 0–4 years, and among these, one can identify those children who were aged less than 1 year (86 cases) or more than 1 but less than 2 years (74 cases) at the time of the catastrophe.

An analysis of the dose-dependence of the incidence rate of thyroid cancer has shown that additional incidence in the age group under study is significantly increasing in the post-latent period in the presence of an exposure dose over 0.5 Gy (Table 3).

A morphological analysis has shown that 92.1% of carcinomas in children are represented by papillary carcinomas. Follicular carcinomas have been revealed in 4.1% and medullary carcinomas in 3.2% of cases. Papillary carcinomas in children throughout the periods of follow-up were most often (more than 70% of cases) characterized by a

Table 3
Thyroid cancer incidence per 10^5 person-years and excess incidence by observation period and thyroid dose for children (aged 0–14 at the time of surgery) in the five northern regions of Ukraine

Thyroid[a] dose (Gy)	Observation period							
	1986–1989		1990–1992		1993–1995		1996–1998	
	Incidence	Excess incidence[b]	Incidence	Excess incidence[b]	Incidence	Excess incidence[b]	Incidence	Excess incidence[b]
0.01–0.05	0.13	0.03	0.23	0.09	0.33	0.16	0.57	0.35
0.05–0.1	0.20	0.10	0.92	0.78	1.49	1.32	1.59	1.37
0.1–0.3	0.00	0.00	1.43	1.29	4.44	4.27	2.90	2.68
0.3–0.5	0.00	0.00	1.64	1.50	4.06	3.89	4.94	4.72
0.5–1.0	0.00	0.00	6.43	6.29	5.74	5.57	12.90	12.68
1.0	0.00	0.00	5.83	5.69	20.93	20.76	29.17	28.95

[a] Each dose class includes left end and excludes right end.

[b] Excess incidence = incidence – baseline incidence; baseline incidence for children aged 0–14 at the time of surgery was estimated for age distribution of Ukraine in 1989 (census data) as varying from 0.1 case per 10^5 person-years in 1986–1989 up to 0.22 cases per 10^5 person-years in 1996–1998.

solid–follicular structure; but in the last years (1999–2000), an increase in the rate of tumors with typical papillary structure (20.6%) as compared to the previous periods of follow-up were noted [7,9,14]. In addition, tumors with papillary–follicular structure (2.9%) or papillary–solid structure (8.8%) were more often reported.

Metastases of papillary carcinoma to cervical lymph nodes have been reported in children operated at our institute in 62.0% of cases. Metastases appeared most often in children in the presence of solid–follicular structures of papillary carcinoma in 72% of cases.

4. Discussion

A significant rise in thyroid cancer in children after the Chernobyl catastrophe represented a basis for performing deepened studies of these tumors in the framework of international programs involving leading research centers. Large-scale investigations using methods of immunohistochemistry and in situ hybridization have been conducted by our institute together with the University of Cambridge (UK) in this field beginning 1994, and clearing up possible morphological features of thyroid carcinomas in children was a top priority task, because the morphology of any tumor is closely related to the molecular–biological changes involved in its genesis.

It has been established that the most frequent subtype of dominant papillary carcinoma was represented by the solid–follicular one, which occurred in children from the Ukraine 2.2 times more frequently than in children of Great Britain who were considered as a control group having not undergone the aftereffects of the Chernobyl accident [4,7]. It has also been shown that the relative risk of developing papillary carcinoma with solid–follicular structure in children rose with increasing thyroid exposure dose [14].

Hence, it appears that we should first of all take into consideration the peculiarities of immunohistochemical changes in thyroid carcinomas of just solid–follicular structure. We have studied a wide spectrum of growth factors and oncogens involved in thyroid carcinogenesis [4,7,15]. In particular, the differences found in the localization in tumoral cells of one of the most important factors in the development of papillary carcinoma, ret-oncogen, depend on the histological structure of the tumor which served as a basis for starting molecular–biological investigations of the expression and translocations in this gene using the RT-nPCR. The molecular–biological investigations of papillary carcinomas performed on children of the Ukraine and Belarus allowed us to establish that rearrangements in ret-gene are closely related to the histological subtype of the papillary carcinoma, and the solid–follicular variant of the tumor is mainly characterized by PTC3 translocation, and classical papillary or diffuse-sclerosing variant by PTC1 translocation [16–18].

Taking into account that the tumors with solid–follicular structure are the most frequent in children of Ukraine and Belarus following the Chernobyl accident, it may be suggested that PTC3 translocations of ret-gene would be associated with the development of radiation-induced thyroid cancer, but additional investigations are needed to prove such a hypothesis.

Thus, numerous literature data and our investigations point out that the problem of post-Chernobyl thyroid cancer will remain a topical one for many years. This will include search of new tumoral markers, clearing up additional ways of intracellular transfer of signal, and analysis of molecular–biological disturbances in different thyroid carcinomas, which will lead as a whole to the development of additional diagnostic criteria and to improvement of the methods of treatment of thyroid cancer.

Based on the above data, it is evident that the radiation factor plays an important role in the development of malignant tumors of the thyroid gland in children. Taking into account that the Chernobyl catastrophe, as we have pointed out, differs to a large extent—as to the spectrum of released radionuclides and character of health aftereffects—from previous radiation accidents in the world, in particular, in Japan and the Marshall Islands, investigations of the incidence, geographical distribution, and morphological features of post-Chernobyl thyroid carcinomas depend on the age of the child at the time of the accident and will remain topical ones for many years. Currently, these studies included follow-up of children, in the following years, follow-up of adolescents and adults who were exposed to radiation in their childhood and kept for all their life the sad title of "Chernobyl children."

References

[1] V.S. Kazakov, E.P. Demidchik, L.N. Astakhova, Thyroid cancer after Chernobyl, Nature 359 (1992) 21.
[2] E.D. Williams, Chernobyl, eight years on, Nature 371 (1994) 556.
[3] I.A. Likhtarev, B.G. Sobolev, I.A. Kairo, N.D. Tronko, T.I. Bogdanova, V.A. Oleinic, E.V. Epshtein, V. Beral, Thyroid cancer in the Ukraine, Nature 375 (1995) 365.
[4] E.D. Williams, N.D. Tronko (Eds.), Molecular, Biological Characterization of Childhood Thyroid Cancer, Final Report, Brussels–Luxemburg, 1996, pp. 1–105.
[5] E.P. Demidchik, A.F. Tsyb, E.F. Lushnikov, Thyroid Cancer in Children (After-Effects of the Chernobyl Accident), Meditsina, Moscow, 1996.
[6] S. Yamashita, M. Ito, H. Namba, T. Hara, K. Ashizawa, T. Nishikawa, M. Hoshi, Y. Shibata, S. Nagataki, K. Kiikuni, Screening for childhood thyroid diseases around Chernobyl, in: S. Nagataki, S. Yamashita (Eds.), Nagasaki Symposium, Radiation and Human Health, Proposal from Nagasaki, Excerpta Med. Int. Congr. Ser., vol. 1103, 1996, pp. 103–116.
[7] N.D. Tronko, T.I. Bogdanova, Thyroid Cancer in Children of Ukraine (After-Effects of the Chernobyl Accident), Chernobylinterinform, Kiev, 1997.
[8] P. Jacob, G. Goulko, W.F. Heidenreich, I. Likhtarev, I. Kairo, N.D. Tronko, T.I. Bogdanova, J. Kenigsberg, E. Buglova, V. Drozdovitch, A. Golovneva, E.P. Demidchik, V. Beral, Thyroid cancer risk to children calculated, Nature 392 (1998) 31–32.
[9] M.D. Tronko, T.I. Bogdanova, I.V. Komisarenko, O.V. Epstein, V.A. Oliynyk, A.Ye Kovalenko, I.A. Likhtarev, I.A. Kairo, S.B. Peters, V.A. LiVolsi, Thyroid carcinoma in children and adolescents in Ukraine after the Chernobyl accident: statistical data and clinicomorphologic characteristics, Cancer 86 (1999) 149–156.
[10] A.F. Tsyb, V.V. Shakhtarin, E.F. Lushnikov, V.F. Stepanenko, V.P. Snykov, E.M. Parshkov, S.F. Trofimova, Development of cancer and non-cancer thyroid diseases in children and adolescents after the Chernobyl accident, in: G. Thomas, A. Karaoglou, E.D. Williams (Eds.), Radiation and Thyroid Cancer, World Scientific, Singapore, 1999, pp. 79–88.
[11] B.M. Dobyns, B.A. Hyrmer, The surgical management of benign and malignant thyroid neoplasm in Marshall Islanders exposed to hydrogen bomb fallout, World J. Surg. 16 (1992) 126–140.
[12] H. Ezaki, Thyroid cancer, in: I. Shigematsu (Ed.), Effects of A-Bomb Radiation on the Human Body, Bunkodo, Tokyo, 1995, pp. 70–79.
[13] Sh. Nagataki, Atomic bomb survivors population, in: G. Thomas, A. Karaoglou, E.D. Williams (Eds.), Radiation and Thyroid Cancer, World Scientific, Singapore, 1999, pp. 35–40.

[14] T. Bogdanova, V. Kozyritsky, M. Tronko, I. Likhtarev, I. Kairo, M. Chepurnoy, V. Shpak, Morphological features and analysis of radiation risk of development of post-Chernobyl thyroid carcinoma in children and adolescents of Ukraine, in: G. Thomas, A. Karaoglou, E.D. Williams (Eds.), Radiation and Thyroid Cancer, World Scientific, Singapore, 1999, pp. 151–154.
[15] T. Bogdanova, L. Zurnadzhy, M. Tronko, G.A. Thomas, E.D. Williams, Characterization of lymphoid infiltration in post-Chernobyl childhood thyroid carcinoma in Ukraine, in: G. Thomas, A. Karaoglou, E.D. Williams (Eds.), Radiation and Thyroid Cancer, World Scientific, Singapore, 1999, pp. 213–216.
[16] G.A. Thomas, H. Bunnell, E.D. Williams, M. Santoro, G. Vecchio, T.I. Bogdanova, L. Voskoboinik, N.D. Tronko, V. Pozcharskaya, E.D. Cherstvoy, Association between morphological subtype of post-Chernobyl papillary carcinoma and rearrangement of the RET oncogene, in: G. Thomas, A. Karaoglou, E.D. Williams (Eds.), Radiation and Thyroid Cancer, World Scientific, Singapore, 1999, pp. 255–267.
[17] G.A. Thomas, H. Bunnell, H.A. Cook, E.D. Williams, A. Nerovnya, E.D. Cherstvoy, N.D. Tronko, T.I. Bogdanova, G. Chiaetta, G. Viglietto, F. Pentimalli, G. Salvatore, A. Fusko, M. Santoro, G. Vecchio, High prevalence of RET/PTC rearrangements in Ukrainian and Belarussian post-Chernobyl thyroid papillary carcinomas: a strong correlation between RET/PTC3 and the solid–follicular variant, J. Clin. Endocrinol. Metab. 84 (11) (1999) 4232–4238.
[18] M. Santoro, G.A. Thomas, G. Veccio, G.H. Williams, A. Fusko, G. Chiapetta, V. Pozcharskaya, T.I. Bogdanova, E.D. Cherstvoy, L. Voskoboinik, N.D. Tronko, A. Carss, H. Bunnell, M. Tonnachra, J. Parma, J.E. Dumont, G. Keller, Gene rearrangement and Chernobyl related thyroid cancer, Br. J. Cancer 82 (2000) 315–322.

International Congress Series 1234 (2002) 85–93

Risk of radiogenic thyroid cancer in the population of the Bryansk and Oryol regions of Russia after the Chernobyl accident (1991–1998)

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Abstract

The manuscript presents results of the radiogenic thyroid cancer risk analysis in the Bryansk and Oryol regions among children and adolescents at exposure (0–17 years of age). A total of 170 cases of thyroid cancer were diagnosed from 1991 to 1998. Of these, 106 cases were in the Bryansk and 64 in the Oryol region. The size of the exposed population under study is 374 447 persons in the Bryansk region and 207 592 persons in the Oryol region (data of the 1989 census). The mean thyroid dose from incorporated isotopes of ^{131}I for children and adolescents at exposure is 0.071 Gy in the Bryansk region and 0.013 Gy in the Oryol region. The method of maximum likelihood for nonstationary Poisson series of events was used for risk calculation. The analysis focuses on the relationship between thyroid cancer incidence and thyroid dose due to incorporated iodine radioisotopes. The calculations were based on personal data about disease cases and demographic and dose information for the population points in the regions under study. Statistically significant excess of thyroid cancer incidence above the spontaneous rate was obtained for children and adolescents of the Bryansk region. The excess relative risk per unit dose of 1 Gy (ERR_{1Gy}) with 95% confidence intervals is 11.9 (7.2, 16.6). For children and adolescents of the Oryol region between 1991 and 1998 statistically significant excess risk was not detected: 6.5 (−20.2, 30.2). The value of the standardized ratio of spontaneous thyroid cancer incidence in the region to the general incidence in Russia is 3.5 with 95% confidence intervals (2.8, 4.2) for the Bryansk region. For the Oryol region this ration is 5.3 (4.0, 6.6). The excess of spontaneous incidence observed in the study areas is primarily due to regional differences in incidence and registration features (screening effect). The attributive risk of induction of radiogenic cancers among children and adolescents in the Bryansk region is 46%. This mean that one of every two thyroid cancers detected in the Bryansk

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PII: S0531-5131(01)00598-2

region between 1991 and 1998 are radiation induced.

Keywords: Thyroid cancer; Radiation risk; Children; Chernobyl

1. Introduction

After the Chernobyl accident, an essential growth of thyroid cancer incidence in the contaminated areas of Russia, Ukraine and Belarus has occurred. One of the potential causes of the increase is exposure of thyroid gland to incorporated iodine-131 (^{131}I). This is a particular concern for those who were children and adolescents at the exposure, as the risk of developing thyroid cancer (as well as dose) is strongly dependent on age at exposure.

There are a large number of publications on radiation induced thyroid cancer after the Chernobyl accident. Most results of these studies have been described in Ref. [1].

The work [1] focuses primarily on descriptive approaches limited by analysis of incident rate and standardized incidence ratio (SIR).

Among the above-mentioned works devoted to analysis to thyroid cancer incidence after the Chernobyl accident, we refer, for example, to Refs. [2–5].

2. Material and methods

2.1. Study area and population

The basic demographic characteristics of the studied population are presented in Table 1.

Gender and age distribution in the territorial units were calculated under the assumption that this distribution is identical with the distribution of a rayon, in which this population point is located. A total of 3085 and 2916 population points were considered in the Bryansk and Oryol region, respectively, the population of which accounts for 99.9% of the whole population of these regions.

Table 1
The results of risk estimation for the population under consideration (age at exposure 0–17 years)

Region	Bryansk	Oryol
Sex	Both	Both
Size	374 447	207 592
Mean dose (Gy) healthy/cases	0.071/0.15	0.013/0.009
ERR/Gy (95% CI)	11.8 (7.2, 16.6)	6.4 (−20.2, 30.1)
Coefficient *f* (95% CI)	3.5 (2.8, 4.2)	5.3 (4.0, 6.6)

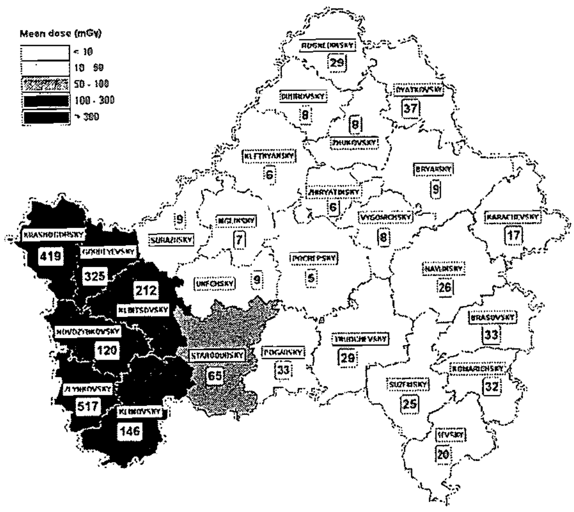

Fig. 1. Geographical pattern of thyroid doses for children and adolescents aged 0–17 years at exposure (Bryansk region).

2.2. Thyroid doses in the Bryansk region

The personified mean thyroid doses for the population of the Oryol region were calculated based on the "Methodology for reconstruction of thyroid dose from iodine radioisotopes in residents of the Russian Federation exposed to radioactive contamination

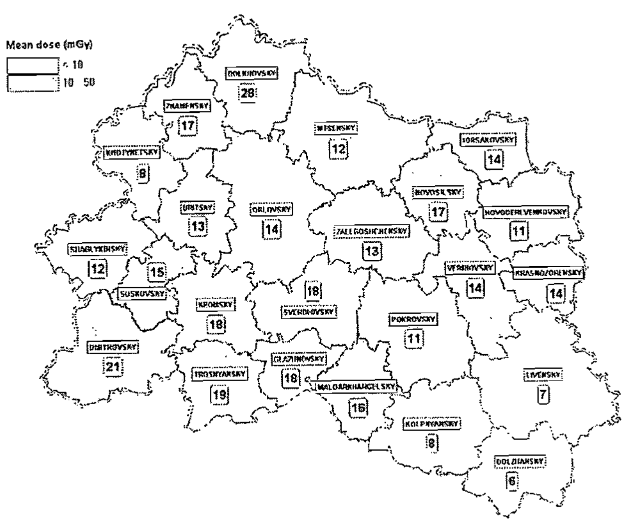

Fig. 2. Geographical pattern of thyroid doses for children and adolescents aged 0–17 years at exposure (Oryol region).

as a result of the Chernobyl accident in 1986," the latest revision of which was issued on 31 May 2000.

Results of the calculation are shown in Figs. 1 and 2 as a map of thyroid dose distribution among children and adolescents in the Bryansk and Oryol regions.

The thyroid dose was determined using the dependence of dose on age at exposure and residence address at exposure time (the name of the population point). The basic dosimetric data for the studied cohort are shown in Table 1.

2.3. Registration of thyroid cancer cases

These are official data of oncological dispensaries in the Bryansk and Oryol regions which were in charge of registration of cancer patients in accordance with regulations of the Ministry of Health of Russia.

Information used in the analysis of dose response includes date of birth, gender, address of residence at exposure, date of diagnosis or surgery and thyroid dose from incorporated iodine radioisotopes.

2.4. Background incidence rate of thyroid cancer

In Russia annual medical check-ups were started shortly after the accident to survey children for thyroid disease. Examination included palpation, ultrasound examination and thyroid hormone testing.

In calculating dynamics of thyroid cancer, spontaneous rate of Russia from 1989 to 1998 was used.

2.5. Risk analysis

As the background rate varies with time, the nonstationary Poisson series of events to model incidence was used in the risk analysis.

The likelihood function for model under consideration is:

$$L = \prod_{i=1}^{n} \lambda_i(t_i) \cdot e^{-\int_0^{t_i} \lambda_i(\tau)\mathrm{d}\tau \cdot} \cdot \prod_{j=1}^{N} e^{-\int_0^{t_j} \lambda_j(\tau)\mathrm{d}\tau \cdot},$$

where n is the number of cases; N is the number of healthy persons; parameter λ_i for a persons i is a function of age at exposure (i), time since exposure (t_i) and absorbed dose (d_i); t_i is time interval from the accident time to detection of case, for healthy persons is time interval from the accident time to the end of 1998.

Excess relative risk per 1 Gy (β) was determined under assumption of linear dependence of the thyroid cancer incidence rate on dose:

$$\lambda_i(t) = \lambda_i^0(t) \cdot f \cdot (1 + \mathrm{ERR}_{1Sv} \cdot d_i),$$

where $\lambda_i^0(t)$ is the spontaneous incidence rate of the thyroid cancer in Russia for attained age (e+t) at the time t, for person i. f is the factor taking into account the

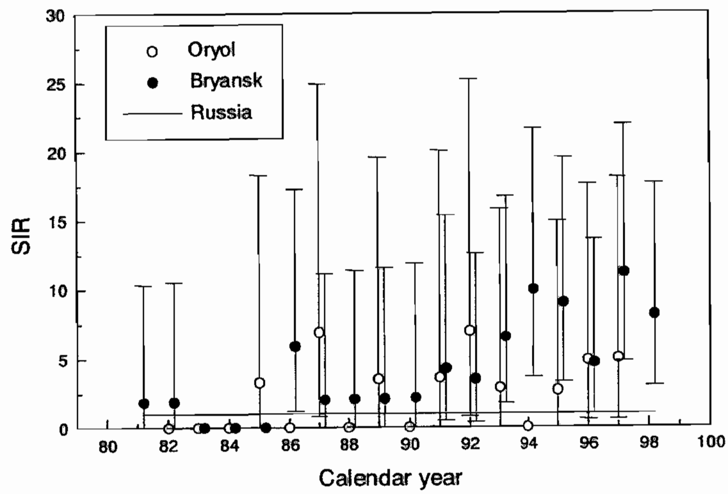

Fig. 3. The dynamics of standardized incidence ratio (SIR) for males 0–29 years of age.

difference between incidence in the considered region and Russia as a whole (function of sex). This difference can be attributed to both the differences in screening effect levels for the population in general and to the difference in actual incidence levels in the study area. It is supposed that the shape of the incidence age distribution in Russia and in the region under study is identical. d_i is the absorbed dose in the thyroid gland for the ith person; ERR_{1Sv} is excess relative risk per unit dose. This value is a function of age at exposure.

The obtained model parameters ERR_{1Sv} and f are used for prediction of the cumulative mortality in the next 5–10 years.

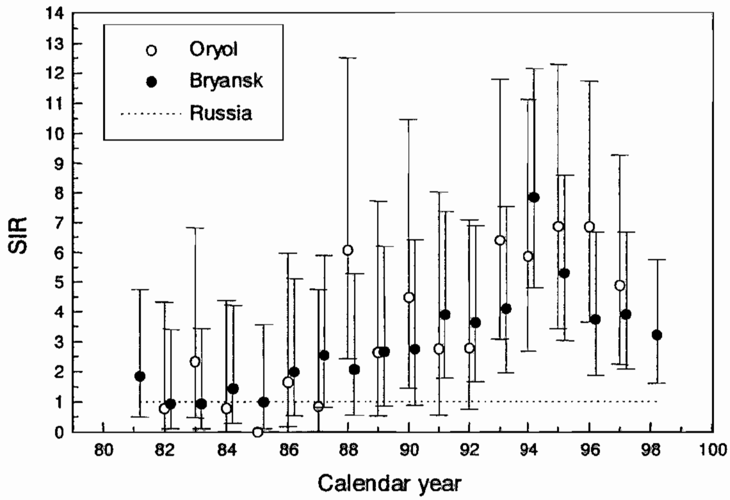

Fig. 4. The dynamics of standardized incidence ratio (SIR) for females 0–29 years of age.

3. Results

Results of estimation of the SIR for thyroid cancers in the studied groups are presented in Figs. 3 and 4.

The above distributions show a common trend. Up to 1986 the SIR is close to 1, i.e., the incidence rate in these regions is close to the general Russian value. In 1986, the SIR increases and remains to be nearly constant to the spring of 1990. The time interval from 1981 to 1990 is the period of appearance of spontaneous cancers (with allowance for the latent period of 5 years from 1986 to 1990). The increase in incidence relative to the control in this time interval can be explained only by the screening effect: better registration of diseases due to wider coverage by specialized medical examination, higher attendance of patients and higher quality of check-ups.

An increase in the incidence rate in the age group 0–29 years after 1990 can be explained by two reasons: the mentioned screening effect and induction of radiogenic cancers. As was pointed out above, this age group has a higher radiation sensitivity and thyroid doses from incorporated ^{131}I.

To answer the question about influence of the radiation factor on thyroid incidence growth, one should first of all analyze the dependence "dose–effect." For solving this problem, knowledge of dose distribution among exposed persons is required. To reconstruct radiation doses, results of directly measured activities of radionuclides are required. These data often are not available or absent. However, some characteristics of thyroid exposure allow a better understanding of the dose effect.

The risk of induction of radiogenic cancers at the same dose rate is known to depend on age at exposure. For malignant neoplasms of most localization, the decrease in age at exposure leads to an increase in the risk of cancer. This equally applies to radiogenic

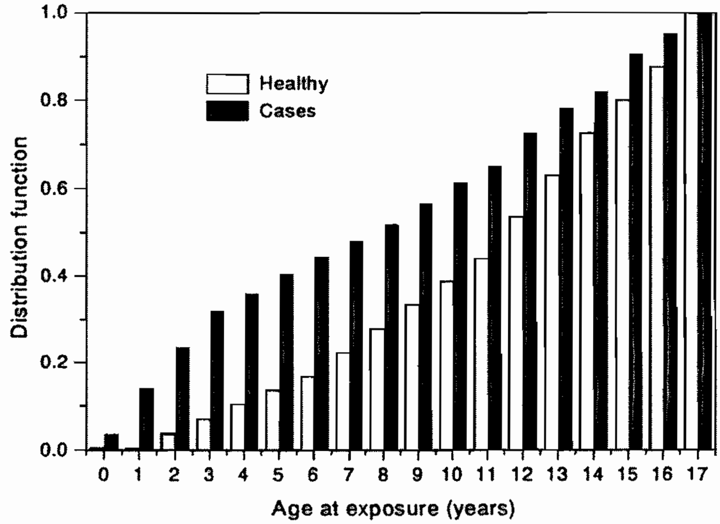

Fig. 5. The relationship between the distribution functions of spontaneous and observed cases of thyroid cancer and age at exposure (the Bryansk region).

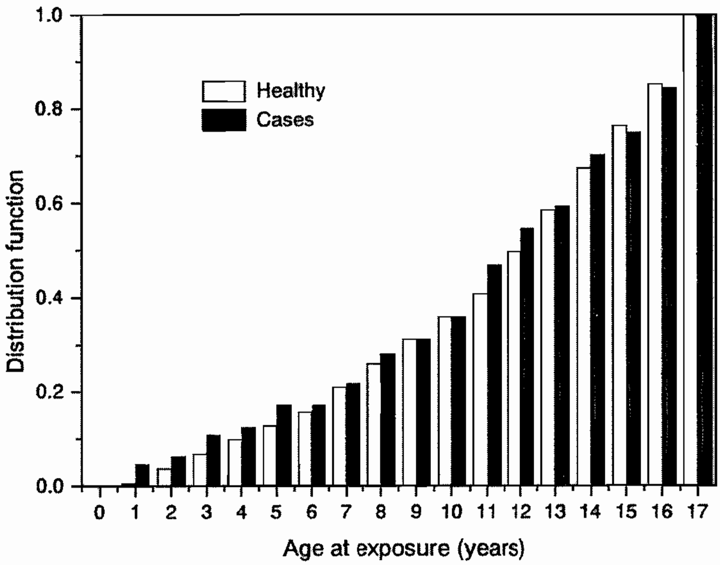

Fig. 6. The relationship between the distribution functions of spontaneous and observed cases of thyroid cancer and age at exposure (the Oryol region).

thyroid cancer. The above risk dependence will be better defined in case of thyroid exposure to incorporated ^{131}I, as in this case, the thyroid exposure dose will depend on age at exposure. Therefore, induction of radiogenic cancers should modify the shape of age distribution of cancers.

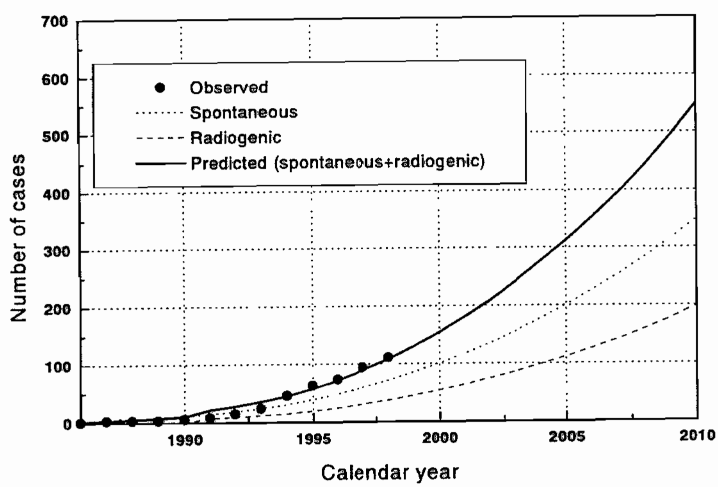

Fig. 7. Prediction of thyroid cancer incidence among children and adolescents after the Chernobyl accident in the Bryansk region.

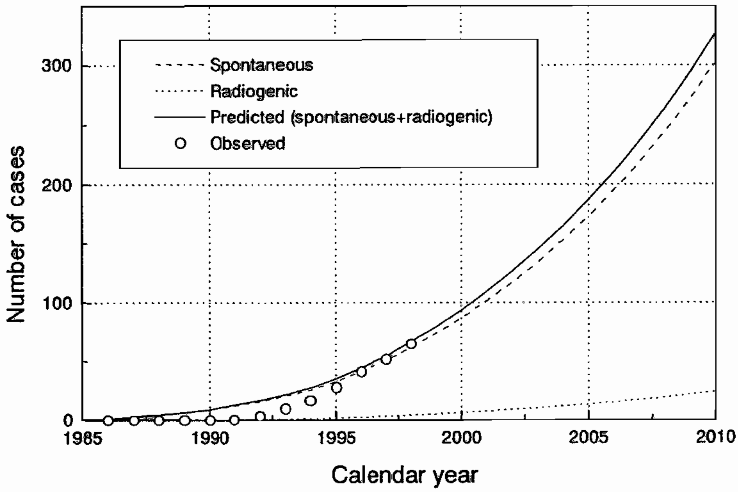

Fig. 8. Prediction of thyroid cancer incidence among children and adolescents after the Chernobyl accident in the Oryol region.

Figs. 5 and 6 present the distribution function of the observed and spontaneous cases in the population under consideration depending on age at exposure.

As can be seen, the age structure has drastically changed for cases among children and adolescents in the Bryansk region. The curve shape is indicative of a considerable increase in incidence for younger ages, as compared with Russia in general. These features of the distribution may be useful for the analysis of thyroid cancer incidence, because absorbed doses are not considered for this purpose. The distributions presented in the figures confirm the conclusions of the regression analysis that there is statistically significant risk for the Bryansk region, but no statistically significant risk for the Oryol region.

Table 1 illustrates the values of the risk coefficients (ERR_{1Gy}) and f coefficient taking into account the difference between incidence in the considered region and Russia as a whole (function of sex) with 95% confidence intervals. The risks for children and adolescents of the Bryansk region appear to be significant.

The spontaneous incidence rate in the considered period differs from the incidence of Russia as a whole by 3–5 times. As stated above, the difference is conditioned by regional variation in incidence and screening effect of thyroid cancer cases.

The results of thyroid cancer prediction are presented in Figs. 7 and 8. As can be seen, the result of prediction using the parameters of model is in good agreement with the observed incidence.

4. Conclusions

The excess relative risk ERR_{1Gy} per unit dose 1 Gy among children and adolescents at Chernobyl accident (0–17 years of age) of the Bryansk region was found in the observation period 1991–1998 to be 11.8 with 95% CI (7.2, 16.6) for both sexes. The risk for the children and adolescents of the Oryol region has not been confirmed. The spontaneous incidence rate in the region under consideration is about 3.5–5 times higher than in Russia as a whole. This excess is attributed to the differences in registration of diseases and regional differences in spontaneous level.

References

[1] G. Thomas, A. Karaoglou, E.D. Williams (Eds.), Radiation and Thyroid Cancer, Proceeding of an International Seminar on Radiation and Thyroid Cancer. World Scientific Publishing, Brussels-Luxembourg, 1999.

[2] V.K. Ivanov, A.I. Gorski, V.A. Pitkevitch, A.F. Tsyb, Risk of radiogenic thyroid cancer in Russia following the Chernobyl accident. in: G. Thomas, A. Karaoglou, E.D. Williams (Eds.), Radiation and Thyroid Cancer, Proceeding of an International Seminar on Radiation and Thyroid Cancer, World Scientific Publishing, Brussels-Luxembourg, 1999, pp. 89–96.

[3] W.F. Heidenreich, Y. Kenigsberg, P. Jacob, E. Buglova, G. Gulko, H.G. Paretzke, E.P. Demidchik, A. Golovneva, Time trends of thyroid cancer incidence in Belarus after Chernobyl accident, Radiat. Res. 151 (1999) 617–625.

[4] P. Jacob, Y. Kenigsberg, I. Zvonova, G. Gulko, E. Buglova, W.F. Heidenreich, A. Golovneva, A.A. Bratilova, V. Drozdovitch, J. Kruk, G.T. Pochtennaja, M. Balonov, E.P. Demidchik, H.G. Paretzke, Childhood exposure due to the Chernobyl accident and thyroid cancer risk in contaminated areas of Belarus and Russia, Br. J. Cancer 80 (9) (1999) 1461–1469.

[5] Methodology for reconstruction of thyroid doses from iodine radioisotopes in residents of the Russian Federation exposed to radioactive contamination as a result of the Chernobyl accident in 1986, Guidelines MU-2.6.1-00b, (in Russian).

International Congress Series 1234 (2002) 95–102

Comments: lessons from the international collaboration

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Abstract

This paper will describe my personal experience in the investigation of childhood thyroid cancer following the Chernobyl nuclear power plant accident. My experience started in 1987 when I was President of the Japanese Society of Nuclear Medicine and held a symposium on "Radiation and the Thyroid" where the health effects of the Chernobyl accident were reported by an expert from the European Thyroid Association (ETA). In 1990, I joined the IAEA project and the Chernobyl Sasakawa Health and Medical Cooperation Project, followed by the WHO/IPHECA Project, and the projects of the Ministry of Foreign Affairs, Japan. In 1992, I participated as a member of the European Community Commission, the Nagasaki Association for Hibakushas' Medical Care (NASHIM), the Hiroshima International Council for Health Care of the Radiation-Exposed (HICARE), and finally as the Chairman of the Radiation Effects Research Foundation (RERF). In addition to a description of the results of each project, the results of a scientific investigation on the health effects of the Chernobyl accident will be summarized and the gap between the scientific results and the public understanding will be discussed. Finally, the study themes to advance scientific knowledge for the benefit of humanity will be suggested.

Keywords: International collaboration; Thyroid cancer; Public understanding; Nagasaki University; Radiation Effects Research Foundation

1. Introduction

Since the previous speakers were experts from each republic, my comments here represent simply my own personal experiences in the investigations of childhood thyroid cancer after the accident of Chernobyl nuclear power plant.

My first involvement was in 1987 when I was President of the Japanese Society of Nuclear Medicine. At the symposium entitled Radiation and the Thyroid, it was reported

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PII: S0531-5131(01)00599-4

by an expert from the European Thyroid Association that there had been an increase of thyroid cancer by 50 cases throughout Europe. The effects of the atomic bomb on thyroid diseases in Nagasaki were also reported.

In 1990, the USSR government requested IAEA to support the International Chernobyl project and the Sasakawa Foundation to carry out the International Chernobyl Sasakawa Project in which Nagasaki University School of Medicine was involved. Since then, our group in Nagasaki University participated in many collaborative works with WHO, EC, NIS countries, and the projects of Ministry of Foreign Affairs, NASHIM and HICARE, Japan. In addition to the description of each project, the results of scientific investigation will be summarized and the dissociation between the scientific results and the public impression will be discussed. Finally, the study themes to further enrich scientific knowledge for the benefit of human beings will be suggested.

2. History of the investigation of the health effects of the Chernobyl Nuclear Plant accident

The history of the investigation of the health effects of Chernobyl Nuclear Plant accident may be divided into a number of periods as follows:

26 April 1986	Chernobyl nuclear power plant accident
1986–1989	information difficult to obtain
1990–1991	exchanges with other countries initiated
1992	case report: childhood thyroid cancer
1992–1994	period of ascertainment
1995	ascertainment and search for causes
1996–present	investigation carried out to the future

3. 1986–1989: Information difficult to obtain

In 1987, one year after the accident in Chernobyl, the annual meeting of the Japanese Society of Nuclear Medicine was held in Nagasaki. Since I was president of the society, I decided on the series of symposia entitled "Radiation and the Thyroid" [1,2].

4. 1990–1991: Exchange with other countries initiated

4.1. Chernobyl Sasakawa Health and Medical Cooperation Project

In August of 1990, the mission of the Chernobyl health and medical cooperation project visited the former USSR for a review of the project. A patient with Graves' disease encountered in Gomel strongly believed that her disease was due to the Chernobyl

Table 1
Chernobyl Sasakawa Project

Subjects	100 000 children aged 0–10 years at the time of the Chernobyl accident
Methods	(A) Thyroid diseases
	based on the same method used for A-bomb survivors in Nagasaki
	(1) history: residential history, case history
	(2) thyroid ultrasonography
	(3) thyroid-related hormone (TSH, free T_4), thyroid auto-antibody
	(4) cytodiagnosis by paracentesis and aspiration
	(B) Hematological diseases
	(C) Dosimetry
	measurement of internal ^{137}Cs exposure dose

Note: protocol was established between August 1990 and May 1991.

accident. After coming back from the USSR, we developed the protocol of the Sasakawa Chernobyl Project (Table 1) based on our experiences in the investigation of atomic bomb survivors in Nagasaki. The instrument of ultrasonography similar to one invented by us for the screening of thyroid diseases of atomic bomb survivors [3] was used in the project.

Within 6 months, we succeeded in remodeling five buses equipped with ultrasonogram, whole-body counter, and hematological analyzer and they were brought to Moscow with the help of President Gorbachev. Since then, investigation in five diagnostic centers have continued having symposium once a year for 5 years.

4.2. WHO/IPHECA Project and the other projects

In 1990, the WHO/IPHECA Project [4] was started mainly with support from the Japanese Government. Furthermore, many international institutes and governments started to support the scientific (and humane) projects related to the Chernobyl accident (Table 2).

5. 1992: Report of cases and presentation of problems

Dr. Demidchik, Head of the Chair, Minsk State Medical Institute in Belarus, came to believe that childhood thyroid cancer has been increasing in Gomel, Belarus, since around

Table 2
Scientific (and human) supports for the Chernobyl nuclear accident: support from international institutes and government

Organization	Year of commencement
IAEA	1990–1991
WHO	1990
EU	1991
Japan	1990
	Government, SMHF and other NGOs
Others	1990–1994
	France, Germany, Italy, Netherlands, UK, USA, etc.

1990, based on the number of the cases on which he performed surgery. With the cooperation of WHO in Europe, Cambridge University, and Pisa University, he published his finding in an international scientific journal [5,6]. This was the first paper published with ascertainment by international experts of the findings reported.

At that time, a decision was made that an EC's mission be sent to Belarus, and I was asked to join the mission, which was composed of about 10 thyroid experts. As we saw one child after another with thyroid cancer at the Research Institute of Thyroid Tumor, all of us in the mission came to agree that we saw more patients with this disease than we had ever seen before. We usually expect to find one such child out of one million children per year in Western countries or Japan.

6. 1992–1994: Period of ascertainment

We all agreed that there were many patients, but the problem was whether or not the Chernobyl accident was the cause. Because of the level of increase, or increase year after year, in the number of patients, the staff at the Research Institute of Thyroid Tumor believed that the accident and the radioactive fallout, particularly radioactive iodine from the accident, had caused the increase in the disease. The EC's mission used the expression "very likely" [7], and the experts from the US (5–10 persons) who were at the meeting with us were opposed to the term "very likely." I was the only Japanese, and my stance was relatively close to that of the US experts. Japanese [8], US, and UK (Oxford) [9] researchers published papers later which said that it was too premature to conclude that the Chernobyl accident was responsible for the increase of cases.

The discussion as to whether or not the increased childhood thyroid cancer is attributable to the Chernobyl accident continued for many years since then, and meetings were held by WHO, IAEA, and EC, and in Japan [10] almost every year (Table 3).

Table 3
Period of ascertainment 1992–1994

Symposium in WHO, EC and IAEA		
1992	WHO	Minsk, Belarus
1993	WHO	Kiev, Ukraine
1994	WHO	Geneva, Switzerland
1994	EC	Vienna, Austria
1994	IAEA	Vienna, Austria
Symposium in Nagasaki City		
1993	Nagasaki University	
1994	Ministry of Education, Japan Endocrine Society, Nagasaki University	

7. 1995: Ascertainment and search for causes

7.1. International organizations

The conference, "Health Effects of the Chernobyl Accident and Other Radiation-Related Accidents" was held at Geneva, Switzerland on 20–23 November 1995 sponsored by WHO [11].

"The 1st International Conference of EC, Belarus, Russia, and Ukraine on the Health Effects of the Chernobyl Accident" was held at Minsk, Belarus on 18–22 March 1996 sponsored by EC [12].

"International Conference Commemorating the 10th Anniversary of the Chernobyl Accident" was held at Vienna, Austria on 8–12 April 1996 sponsored by IAEA [13].

The following are the summary of the reports of these international meetings:

(1) For much of the area contaminated by the accident, the current dose rates (including the additional dose due to the accident) are within the range of doses due to the natural background found in areas of Europe uncontaminated by the accident. As a result, it is unlikely that *future exposure* to contamination from the accident will lead to a detectable increase in cancer incidence. Any proposed remedial measures intended to reduce this dose level further should therefore be carefully evaluated for their effectiveness and their probable economic and psychological impact.

(2) As for demonstrated health effects, acute radiation sickness and early deaths occurred only among the initial responders to the accident. Two hundred and thirty-seven subjects were examined in the hospital and among 134 who showed acute radiation syndrome, 28 died within 3 months.

(3) There has been a substantial increase in the incidence of thyroid cancer, especially in young children. Thyroid cancer in exposed individuals who were children at the time of the accident will most likely be in the form of cancer most likely to be clearly associable

Table 4
Summary of the reports in IAEA/WHO/EC Joint Symposium held 10 years after the Chernobyl accident

People considered to have been exposed	
(1) Power plant workers, firemen, etc.	several hundred subjects
(2) Liquidators	hundreds of thousands
(3) Those exposed to radioactive fallout	4 million
People with demonstrated health effects	
(1) People with symptoms of acute radiation syndrome	134 (237 were hospitalized)
28 died within 3 months	
14 died within the subsequent 10 years (two died of blood disease)	
(2) Childhood thyroid cancer	about 800
three died because of thyroid cancer	
(3) Increase in other diseases including leukemia has not been confirmed	

with the accident. This is because of (1) the high thyroid doses compared with doses to other parts of the body, (2) the vulnerability of children to thyroid cancer and (3) the low incidence otherwise of thyroid cancer, especially in children.

(4) Small but significant increases in the rates of some cancers and other health problems have been reported among the liquidators and among the most heavily exposed people of the public. However, except for thyroid cancer, these apparent increases may be due to the improved medical observation of these groups or from other factors not related to radiation exposure due to the accident.

(5) There may have been a slight rise in the incidence of mental retardation among children exposed in utero. However, no clear interpretation of the figures is yet possible and further study is required.

These results are summarized in Table 4.

7.2. Chernobyl Sasakawa Project

The prevalence of thyroid nodules and cancers in the Chernobyl Sasakawa Project is summarized in Table 5. It should be noted that other than the remarkable increase in the prevalence of thyroid cancer, no significant correlation between the prevalence of thyroid cancer and radiation dose (^{137}Cs either in the body or in soil) could be observed [14].

The following current projects will be presented later in this symposium.

1. Comparison of thyroid cancer incidence in children born before and after the accident, Gomel in the Republic of Belarus.
2. Follow-up of high-risk children of thyroid cancer, Gomel in the Republic of Belarus.

Table 5
Chernobyl Sasakawa Project: prevalence of thyroid nodules and cancers, and the correlation between the prevalence and radiation dose

Center	No. of examined children	Thyroid nodule (‰)	Thyroid cancer (‰)
Belarus			
Gomel	19 790	350 (17.69)	38 (1.92)
Mogilev	13 868	24 (1.01)	2 (0.08)
Russia			
Klincy	20 027	97 (4.84)	8 (0.40)
Ukraine			
Kiev	27 759	48 (1.73)	6 (0.22)
Korosten	29 161	66 (2.26)	9 (0.31)
Total	120 605	585 (4.85)	63 (0.52)
Correlation with radiation dose			
^{137}Cs in body		none	none
^{137}Cs in soil		none	none

Table 6
Thyroid cancer—search for the cause

(1) Radiation dose estimation
(A) Reconstruction of dose
(B) Biological dosimetry
(C) Short half-life ^{131}I, ^{132}I, ^{132}Te; external exposure
(2) Epidemiological methods
(A) Possibility of involvement of ^{131}I and other radionuclides with short half-life
(B) Genetic factors
(C) Confounding factors promoting carcinogenesis
(3) Registry of information on thyroid cancer patients
(A) History of exposure
(B) Clinical image
(C) Pathological diagnosis
(D) Storage of blood and tissue specimens
(4) Molecular biological methods

3. Case–control study of childhood thyroid cancer and investigation of dose relationship with international collaboration, both in the Russian Federation and Republic of Belarus.
4. Post-Chernobyl NIS Thyroid Tissue, Nucleic Acid and Data Bank (NISCTB) in the Russian Federation and Republic of Belarus [15].

8. 1996–present: investigation should be carried out in the future

8.1. Scientific as well as humanitarian projects

1. Search for cause—radiation: external or internal exposure, issue of the nuclide
2. Treatment of childhood thyroid cancer—methods of diagnosis, indication of operation and treatment with radioactive ^{131}I, substitution therapy T4, Vit. D, Ca, etc.
3. Prevention of childhood thyroid cancer—administration of iodine and thyroid hormone Follow-up of high-risk cohorts

Table 6 depicts further issues with regard to “Search for Cause.”

Table 7
Study themes as scientific knowledge—thyroid cancer in Chernobyl

100-fold increase in cancer incidence during several years—unprecedented
Opportunity to elucidate the mechanism of carcinogenesis—unprecedented
Importance of collecting biological materials
Importance of creating database for study subjects
Necessity of international collaborating system
(EU, USA, Japan, WHO)

8.2. Study themes as scientific knowledge

As shown in Table 7, a 100-fold increase of thyroid cancer incidence (or any other cancers) within 4–5 years is unprecedented in the history of medical sciences, and provides a very unique opportunity to elucidate the mechanism of carcinogenesis.

9. Scientists' social responsibility

Scientists should explain the results of scientific study to the general public in a easy-to-understand way. Unnecessary concerns and prejudice should be eradicated.

While seeking the understanding of society, scientists should aggressively conduct studies which are both relevant to the present and hold the promise of advancing scientific knowledge.

Acknowledgements

I would like to express my sincere appreciation to the following for providing me this opportunity: USSR, Republic of Belarus, Russian Federation, Ukraine, UN, WHO, IAEA, UN, USA, EU, UK, etc.

References

[1] Journal of The Japanese Society of Nuclear Medicine 24 (8) (1987).
[2] S. Nagataki, Radiation and the Thyroid, Excerpta Medica, Tokyo, 1989.
[3] N. Yokoyama, Y. Nagayama, F. Kakezono, T. Kiriyama, S. Morita, S. Ohtakara, S. Okamoto, I. Morimoto, M. Izumi, N. Ishikawa, K. Ito, S. Nagataki, Determination of the volume of the thyroid gland by a high resolutional ultrasonic scanner, J. Nucl. Med. 27 (9) (1986) 1475–1479.
[4] G.N. Souchkevitch, A.F. Tsyb (Eds.), Health consequences of the Chernobyl accident. Results of the IPHECA pilot projects and related national programmes. Scientific report. International programme on the health effects of the Chernobyl accident (IPHECA). WHO, Geneva, 1996.
[5] V.S. Kazakov, E.P. Demidchik, L.N. Astakhova, Thyroid cancer after Chernobyl, Nature 359 (6390) (1992) 21.
[6] K. Baverstock, B. Egloff, A. Pinchera, C. Ruchti, D. Williams, Thyroid cancer after Chernobyl, Nature 359 (6390) (1992) 21–22.
[7] D. Williams, A. Pinchera, A. Karaoglou, K.H. Chadwick (Eds.), Thyroid cancer in children living near Chernobyl: expert panel report on the consequences of the Chernobyl accident, European Commission, Brussels, 1993.
[8] I. Shigematsu, J.W. Thiessen, Childhood thyroid cancer in Belarus, Nature 359 (6397) (1992) 681.
[9] V. Beral, G. Reeves, Childhood thyroid cancer in Belarus, Nature 359 (6397) (1992) 680–681.
[10] S. Nagataki (Ed.), Nagasaki Symposium on Chernobyl: Update and Future, Elsevier, Amsterdam, 1994.
[11] S. Nagataki, Radiation and the thyroid. Health consequences of the Chernobyl and other radiological accidents, International Conference, 20–23 November 1995, Geneva.
[12] A. Karaoglou, G. Desmet, G.N. Kelly, H.G. Menzel (Eds.), The Radiological Consequences of the Chernobyl Accident, European Commission, Luxembourg, 1996.
[13] D. Delves, M. Demir, One decade after Chernobyl, Summing up the Consequences of the Accident, International Atomic Energy Agency, Austria, 1996.
[14] S. Yamashita, Y. Shibata (Eds.), Chernobyl: A Decade, Elsevier, Amsterdam, 1997.
[15] G.A. Thomas, E.D. Williams, Thyroid tumor banks, Science 289 (5488) (2000) 2283.

The new Chernobyl Sasakawa Projects

International Congress Series 1234 (2002) 105–113

Joint Belarus/Russia/EU/IARC/SMFH case–control studies of thyroid cancer in young people following the Chernobyl accident

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Abstract

In 1996, following several years of collaborative international studies of the consequences of the Chernobyl accident, a number of groups proposed to carry out case–control studies of thyroid cancer among young people in contaminated territories of Belarus and Russia. Collaborations were set-up between the participants of the Chernobyl Sasakawa Project and of those of the Belarus/Russia/EU/IARC project. These involved joint field work and dose reconstruction, although both projects maintained their original objectives: to evaluate the risk of I-131-induced thyroid cancer and to study the role of possible modifying factors in radiation carcinogenesis, in particular, iodine deficiency and supplementation and genetic predisposition. Joint data collection is now virtually finished and dose reconstruction is nearing completion. Final results are expected in 2002. The current paper summarises the objectives and methods of the case–control studies, as well as the very preliminary

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PII: S0531-5131(01)00600-8

results based on joint data collection and analyses. These appear to indicate that cases were likely to have received higher doses from I-131 on average than controls. The collaboration has resulted in the collection of one of the largest sources of data on thyroid cancer risk in children, adolescents and young adults exposed to ionising radiation. Results from this work are likely to have important implications for radiation protection in general, as well as for public health actions among exposed populations in the CIS.

Keywords: Thyroid cancer; Radiation risk; Risk modifiers; Iodine deficiency; Genetic predisposition; Children; Chernobyl

1. Introduction

Following initial reports of increased thyroid cancer in young people residing in territories contaminated by the radiation from the Chernobyl accident [1–6], a number of international collaborations were set-up in order to verify the increase and evaluate the magnitude of the problem: Chernobyl Sasakawa Health and Medical Cooperation Project [7], European Union (EU) International Scientific Collaboration on the Consequences of the Chernobyl Accident [8,9], WHO International Programme on the Health Effects of the Chernobyl Accident (IPHECA) [10], WHO International Thyroid Project (ITP) [11], International Consortium for Research on the Health Effects of Radiation (ICRHER) [12] and US National Cancer Institute project [13].

In 1996, the results of these collaborations led a number of different organizations to independently plan case–control studies of thyroid cancer in young people in Belarus and

Table 1
Main characteristics of the case–control studies

	Chernobyl Sasakawa Project	EU/Belarus/Russia/IARC
Objectives	• Relationship between I-131 dose and risk of thyroid cancer in young people following Chernobyl accident	• Role of I-131 in thyroid cancer in young people following the Chernobyl accident
	• Estimate the risk per unit radiation dose	• Role of genetic predisposition, stable iodine status, short-lived isotopes of iodine and screening in radiation-induced thyroid cancer
Design	Case–control study	Hybrid case–control and genetic predisposition study
Study areas	• Belarus: Gomel and Mogilev regions	• Belarus: Gomel and Mogilev regions
	• Russia: Bryansk, Kaluga, Orel and Tula regions	• Russia: Bryansk, Kaluga, Orel and Tula regions
Cases	• Belarus: 14 years or less at time of accident	• Belarus: 14 years or less at time of accident
	• Russia: 17 years or less at time of accident	• Russia: 17 years or less at time of accident
Controls	• Matched on age, sex and region	• Matched on age, sex and region
	• Excluding thyroid nodules	• Matched on age, sex and settlement

Russia. These included in particular three proposed studies with overlapping study populations, but differing study objectives: the Chernobyl Sasakawa Project (CSP), the Belarus/Russia/EU/IARC project and the ICRHER project. The objective of the CSP and ICRHER projects was to evaluate the risk of I-131-induced thyroid cancer, while that of the EU/IARC sponsored project was, in addition, to study the role of possible modifying factors in radiation carcinogenesis.

Concerns were raised by the investigators planning these studies and discussed at the 5th Chernobyl Sasakawa symposium in Kiev about the burden on cases of being involved in more than one study. Recommendations were therefore made for concertation and collaboration between different groups. This was followed by meetings between concerned scientists in order to develop a collaboration strategy.

An agreement was reached between the participants in the Chernobyl Sasakawa Project and the Belarus/Russia/EU/IARC project to pool resources and carry out joint field work for both studies, each study retaining its original objectives (see Table 1 for a description of the objectives and study design for both projects). This allowed the broadening of the scope of the two projects. Overlap with the ICRHER project was avoided by agreeing on different periods of case ascertainment in Bryansk oblast in Russia.

The current paper summarises the methods of the joint Belarus/Russia/EU/IARC/SMFH case–control studies, as well as the preliminary results based on the joint data collection.

2. Material and methods

The study population consists of all persons who resided in the two regions of Belarus (Gomel and Mogilev) and were aged 14 years or less at the time of the accident, as well as those who resided in the four regions of Russia (Tula, Orel, Kaluga and Bryansk) and were aged 17 or less.

The cases were patients diagnosed with a histologically verified thyroid carcinoma (not restricted to papillary carcinoma) in the study population between 1 January 1992 and 31 December 1998 and operated in Belarus or Russia.

In Belarus, the study included all prospective cases from Gomel region diagnosed until 31 December 1998 and a sample of retrospective cases, as follows: all cases who were below the age of 2 at the time of the accident and a 50% random sample of all cases who were aged 2 or above, stratified on sex and age. The sampling was done for logistic reasons because of the very large number of cases having occurred in Gomel region. In Mogilev region, all retrospective and prospective cases up to 31 December 1998 were included.

In Russia, the study included all prevalent and new cases from Tula, Kaluga and Orel regions in the study population. In Bryansk oblast, only cases diagnosed between 1 January and 31 December 1998 were included.

All cases were independently verified by a panel of pathologists including one pathologist each from Belarus, Russia, Europe and Japan. The primary sources for retrospective case ascertainment in Belarus were the Belarus Cancer Registry and the records of the Republican Scientific and Practical Center for Thyroid Tumours, completed by the records of the Minsk City Oncological Dispensary. Prospective cases diagnosed on or after 1 April 1998 were identified directly from the Center for Thyroid Tumours. The primary source of ascertainment for cases in Russia was the Russian Medical and Dosimetric Registry (RMDR).

For each case, four population-based controls were selected for the CSP project, matched closely on age (within 1 year for those who were 18 months or older at the time of the accident, within 6 months for aged from 12 to 18 months and within 1 month for those who were less than 12 months), on sex and on region of residence at the time of the accident (26 April 1986). Controls had to be free of thyroid nodule, as determined by ultrasound examination immediately prior to the interview.

In the EU/IARC sponsored project, four population-based controls were also selected. Two were matched closely on age, on sex and on region of residence at the time of the accident (same criteria as above). The other two were matched in the same way on age and sex, but more closely on settlement of residence at the time of the accident. Matching on settlement was carried out to study the possible modifying effect of locally varying factors.

Controls were selected from the population registry—bureau Zapisi Akta Grazhdanskovo Sostoyania (ZAGS) (the office which registers all vital events)—except in Tula and Orel regions of Russia where access to the ZAGS was denied. An alternative solution, using the records from the newly established medical insurance system in these regions, therefore, had to be worked out and tested.

All cases and controls were contacted by letter, informed about the study and given the opportunity of refusing to participate.

Information on variables of interest was obtained using the following approaches:

- a questionnaire administered by a trained interviewer to the subject's mother in the presence of the subject, if he or she was less than 12 at the time of the accident, or to the subject him/herself otherwise;
- ultrasound examinations of thyroid volume of the subject;
- for the EU/IARC sponsored project, further information on possible modifying factors was obtained from medical and school records, results of geographical surveys (of iodine in urine, goitre prevalence, stable iodine content in soil and water), surveys of counter measures and analysis of biological samples (including blood, urine and tumour tissues).

Table 2
Number of cases and controls interviewed by region

	Belarus		Russia				Total
	Gomel	Mogilev	Bryansk	Kaluga	Orel	Tula	
Cases	189	35	11	10	27	22	294
Controls							
Region	745	170	57	40	131	95	1238
Settlement	308	61	17	20	50	27	483
Total	1242	266	85	70	208	144	2015

Table 3
Distribution of age at the time of accident among cases interviewed by region

Age	Belarus		Russia				Percentage of total
	Gomel	Mogilev	Bryansk	Kaluga	Orel	Tula	
<2	71	10	4	1	1	2	30.2
2–4	59	10	3	2	3	5	27.8
5–9	43	5	2	4	6	6	22.3
10–14	16	11	2	3	8	4	14.9
15–18	N.A.	N.A.	0	0	9	5	4.8
Percentage of total	64.1	12.2	3.7	3.4	9.2	7.5	100

N.A.: not available.

Information on the study subjects was collected during joint field missions involving an interview, palpation and ultrasound examination of the thyroid gland of the subject and collection of blood and urine samples.

The primary source of radiation dose considered was I-131, for which individual dose reconstruction is underway. Crude estimation of exposure to shorter-lived isotopes (through the construction of an exposure gradient) is also being carried out, as well as individual estimation of dose from external exposures and from incorporation of long-lived radionuclides.

Dose reconstruction is the responsibility of a joint dosimetry working group, composed of dosimetrists from Belarus, Russia, Germany, Japan and the United States and of the principal epidemiologists in the studies. This working group carried out a critical review of existing methods developed for dose reconstruction in Belarus and Russia, validated these and modified them as appropriate to estimate individual doses using information from the case–control studies. Dose reconstruction and estimation of dosimetric uncertainties are nearly complete.

3. Results

Table 2 shows the number of study subjects interviewed to date by region and case–control status. It should be noted that there are still some interviews to do: approximately

Table 4
Distribution of cases by sex and region

Sex	Belarus		Russia				Total
	Gomel	Mogilev	Bryansk	Kaluga	Orel	Tula	
Male	73	9	6	4	8	8	108
	38.6%	*25.7%*	*54.5%*	*40.0%*	*29.6%*	*36.4%*	*36.7%*
Female	116	26	5	6	19	14	186
	61.4%	*74.3%*	*45.5%*	*60.0%*	*70.4%*	*63.6%*	*63.3%*
Total	189	35	11	10	27	22	294

Columnwise percentages are given in italics.

Table 5
Distribution of subjects by type of settlement of residence at the time of the accident

	Case	Control	Total
Village	135	412	547
	45.9%	*33.3%*	*35.7%*
Town or city	159	826	985
	54.1%	*66.7%*	*64.3%*
Total	294	1238	1532

Columnwise percentages are given in italics.

150 controls need to be reselected and interviewed. The majority of these are settlement controls, which were improperly matched on settlement of residence. All the results presented here therefore concern only region controls, and must be considered as preliminary.

Table 3 shows the distribution of age at the time of the accident among cases, by study region. As anticipated, the largest number of cases came from the region of Gomel. It is noted that cases tended to be older in the regions of Kaluga, Orel and Tula than in Belarus or in Bryansk region. Table 4 shows the distribution of cases by sex and by region. There was a higher proportion of girls than boys with thyroid cancer everywhere except in Bryansk region (although the latter result is based on relatively few cases). The highest proportion of girls among cases was seen in Mogilev and Orel regions.

Table 5 shows the type of settlement of residence at the time of the accident. The proportion of persons living in rural settlements at the time of the accident was significantly greater among cases than among controls (OR=1.7; 95% CI: 1.3–2.2; $p<0.001$). This is supported by the observation that a higher proportion of cases than controls resided in wooden houses—39.46% of cases vs. 25.93% of controls, $p<0.001$ (see Table 6).

Table 7 shows the distribution of the source of milk among cases and controls who consumed milk at the time of the accident. The proportion of persons drinking milk from

Table 6
Distribution of cases and controls by type of dwelling at the time of the accident

Dwelling type	Case	Control	Total
Wood	116	321	437
	39.5%	*25.9%*	*28.5%*
Brick or concrete block	165	884	1049
	56.1%	*71.4%*	*68.5%*
Other	13	22	35
	4.4%	*1.8%*	*2.3%*
Don’t know	0	11	11
	0.0%	*0.9%*	*0.7%*
Total	294	1238	1532

Columnwise percentages are given in italics.

Table 7
Distribution of cases and controls by source of milk among those who consumed milk at the time of the accident

Source of milk	Case	Control	Total
Private cow	162	523	685
	60.9%	*49.8%*	*52.0%*
Other	104	528	632
	39.1%	*50.2%*	*48.0%*
Total	266	1051	1317

Columnwise percentages are given in italics.

private cows at the time of the accident was significantly greater among cases than controls (OR=1.6; 95% CI: 1.2–2.1; $p<0.001$).

4. Discussion

It is too early to draw final conclusions from the data collected jointly under the CSP and EU/IARC sponsored projects, as some controls still need to be reselected and the reconstruction of individual doses is not yet complete.

The preliminary results shown here, nevertheless, are compatible with the hypothesis that cases may have received, on average, higher doses from iodine isotopes than controls. Indeed, for persons residing in rural settlements in these regions of Belarus and Russia, a considerable part of the diet generally comes from milk and milk products from private cows. Further, in a given area, the radioactive iodine content of the milk will be higher, in general, in fresh milk from local cows than in the milk sold commercially because of the additional time between the source and the consumer and the consequent decay in iodine isotopes in the milk.

Individual dose estimates should be available in late 2001 and first publication of results should follow shortly thereafter. It should be stressed that this work currently represents one of the largest collections of data on thyroid cancer in children, adolescents and young adults (up to the age of 30 years) exposed to ionising radiation. It includes nearly 300 cases and over 1700 controls who were children or adolescents at the time of the accident in 1986. Eighty-nine cases and about 400 controls were below the age of 2 years at exposure. The majority of the thyroid cancer cases were diagnosed before the age of 15 years.

Planned analyses will address the following:

• Providing more precise information on dose–response of thyroid cancer risk related to I-131 exposure in young people.

• Evaluating the role of a number of possible modifying factors in radiation carcinogenesis; these include: iodine deficiency and supplementation, age at exposure, genetic predisposition, diet, reproductive factors in women as well as previous history of thyroid and endocrine diseases.

The role of other types of radiation (external radiation, short-lived isotopes of iodine and tellurium and long-lived radionuclides) in the observed increase in thyroid cancer among young people following the Chernobyl accident will also be evaluated, as well as the importance of screening in the detection of these cases.

Because of the rarity of this disease, the observed increase in thyroid cancer incidence in children and adolescents in contaminated areas of the former USSR following the Chernobyl accident is a unique opportunity to evaluate the effects of I-131 on cancer risk in young people, to identify factors which modify radiation risks and to quantify their effects. These were the objectives of the CSP and EU/IARC sponsored projects and the results of these projects are likely to have important implications both for radiation protection of patients and the general population in the case of future accidents. They will also allow more focused public health actions among exposed populations, helping to further identify high-risk groups for possible screening and preventive actions.

5. Conclusions

The collaboration in field work and dosimetry between the CSP and EU/IARC sponsored projects has resulted in one of the largest collection of data on thyroid cancer risk in young people exposed to ionising radiation to date. Preliminary analyses appear to indicate that cases were likely to have received higher doses from I-131, on average, than controls. Dose–response analyses and study of the role of possible modifying factors will start shortly and results are likely to have important implications both for radiation protection in general and for public health planning in the regions contaminated by the Chernobyl accident.

Acknowledgements

This work was made possible due to the support and funding from the Sasakawa Memorial Health Foundation, the European Union (Contracts No. FI4CCT960014, ERB IC15-CT96-0304), the Ministries of Public Health of Belarus and Russia, the Belarussian State Committee for Chernobyl Affairs and the Ministry of Russian Federation on Matters of Civil Defense, Emergency Situations and Liquidation of Consequences of Catastrophies. The assistance of the Public Health Care Administrations of each of the participating regions and of the local and regional population registry offices is gratefully acknowledged.

References

[1] V.S. Kazakov, E.P. Demidchik, L.N. Astakhova, Thyroid cancer after Chernobyl [letter], [see comments]-Nature 359 (1992) 21.
[2] European Commission, Thyroid cancer in children living near Chernobyl. Expert panel report on the consequences of the Chernobyl accident, in: D. Williams, A. Pinchera, A. Karaoglou et al. (Eds.), European Commission Publication EUR 15248. Luxembourg: European Commission, 1993.
[3] I.A. Likhtarev, B.G. Sobolev, I.A. Kairo, N.D. Tronko, T.I. Bogdanova, V.A. Oleinic, E.V. Epshtein, V. Beral, Thyroid cancer in the Ukraine, Nature 375 (1995) 365.
[4] N.D. Tronko, Y. Epstein, V. Oleinik, T. Bogdanova, I. Likhtarev, G. Gulko, I. Kairo, B. Sobolev, Thyroid gland in children after the Chernobyl accident (yesterday and today), in: S. Nagataki (Ed.), Nagasaki Symposium on Chernobyl: Update and Future, Elsevier, Amsterdam, 1994, pp. 31–46.

[5] V.A. Stsjazhko, A.F. Tsyb, N.D. Tronko, G. Souchkevitch, K.F. Baverstock, Childhood thyroid cancer since accident at Chernobyl, Br. Med. J. 310 (1995) 801.
[6] A.F. Tsyb, E.M. Parshkov, V.K. Ivanov, V.F. Stepanenko, E.G. Matveenko, Y.D. Skoropad, Disease indices of thyroid and their dose dependence in children and adolescents affected as a result of the Chernobyl accident, in: S. Nagataki (Ed.), Nagasaki Symposium on Chernobyl: Update and Future, Elsevier, Amsterdam, 1994, pp. 9–19.
[7] Sasakawa Memorial Health Foundation, Chernobyl: a decade, in: S. Yamashita, Y. Shibata (Eds.), Proceedings of the Fifth Chernobyl Sasakawa Medical Cooperation Symposium, Kiev, Ukraine, 14–15 October 1996, Elsevier, Amsterdam, 1997.
[8] European Commission, Experimental Collaboration Project No. 7: epidemiological investigations including dose assessment and dose reconstruction, Final Report, in: H. Storm, A. Okeanov (Eds.), European Commission Publication EUR 16537 EN. Luxembourg: European Commission, 1996.
[9] E. Cardis, A.E. Okeanov, What is feasible and desirable in the epidemiologic follow-up of Chernobyl, in: A. Karaoglou, G. Desmet, G.N. Kelly, H.G. Menzel (Eds.), The Radiological Consequences of the Chernobyl Accident. Proceedings of the First International Conference, Minsk, Belarus, March 1996; European Commission Publication EUR 16544. Luxembourg: European Commission, 1996, pp. 835–850.
[10] World Health Organisation, Health consequences of the Chernobyl accident. Results of the IPHECA pilot projects and related national programmes. Scientific report, in: G.N. Souchkevitch, A.F. Tsyb (Eds.), World Health Organization, Geneva, 1996.
[11] K. Baverstock, E. Cardis, The WHO activities on thyroid cancer, in: A. Karaoglou, G. Desmet, G.N. Kelly, H.G. Menzel (Eds.), The Radiological Consequences of the Chernobyl Accident. Proceedings of the First International Conference, Minsk, Belarus, March 1996; European Commission Publication EUR 16544. Luxembourg: European Commission, 1996, pp. 715–726.
[12] ICRHER, Radiation injury and the Chernobyl catastrophe, in: N. Dainiak, W. Schull, L. Karkanitsa, O. Aleinikova (Eds.), Proceedings of the Conference on Biological Effects of Radiation Injury, Minsk, Belarus, March 22–25 1996. International Consortium for Research on the Health Effects of Radiation. Supplement to Stem Cells, AlphaMed Press, Miamisburg, OH, USA, 1997.
[13] G. Beebe, Epidemiologic studies of thyroid cancer in the CIS, in: A. Karaoglou, G. Desmet, G.N. Kelly, G. Menzel (Eds.), The Radiological Consequences of the Chernobyl Accident, Proceedings of the First International Conference, Minsk, Belarus, March 1996, European Commission EUR 16544, Luxembourg: European Commission, 1996, pp. 731–740.

International Congress Series 1234 (2002) 115–120

I-129 and I-131 ground deposition densities are correlated in Belorussian settlements contaminated following the Chernobyl accident

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Abstract

Long-living I-129 is considered as the witness of short-living I-131 fallout following the Chernobyl accident. Data on I-129 deposition densities might help to estimate thyroid doses in population of many contaminated areas where information on the I-131 ground deposition density is unknown. This pilot study aimed to investigate the correlations between I-129 ground deposition densities measured in 2000 and those of I-131 measured in 1986. I-129 measurements were performed by iodine separation and registration of I-129 decays using beta-x coincidence. Soil samples were collected and I-129, Cs-137 ground deposition densities were measured in three contaminated raions of Belorussia (14 locations in 12 settlements). For 10 of 12 settlements, there were available data of I-131 and Cs-137 spectrometric measurements during the first weeks after the accident in 1986. Results of I-129 and Cs-137 measurements in 2000 were used for the reconstruction of I-131/Cs-137 ratio. Comparisons of reconstructed I-131/Cs-137 ratios with the I-131/Cs-137 ratios obtained by direct measurements in 1986 showed good agreement: correlation coefficient was 0.69 and linear regression coefficient ($\pm$SD) was 2.36($\pm$0.88). The study confirms the possibility to apply the data on I-129 ground deposition densities for further application to

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PII: S0531-5131(01)00601-X

improve estimations of thyroid absorbed doses, which result from I-131 irradiation.

Keywords: Chernobyl accident; I-129; I-131; Thyroid dose

1. Introduction

Thyroid dose estimations in contaminated settlements are very important for medical care and epidemiological studies of the thyroid cancer cases following the Chernobyl accident [1–3]. The lack of information concerning the I-131 ground deposition densities in many settlements of Chernobyl areas in Belorussia and Russia prevents the correct thyroid dose estimation [4]. Uncertainties of thyroid dose estimations, which were based only on Cs-137 contamination, data can reach the value of two orders of magnitude due to a very big variation of I-131/Cs-137 ratios of ground deposition densities in the contaminated areas (ranged from approximately 1 to 100 [5]).

The fallout of long-living I-129 (half-life of 1.6×10^7 years) is considered as the witness of short-living I-131 fallout following the Chernobyl accident [6]. The information on I-129 ground deposition densities might help to estimate thyroid doses in the population of many contaminated areas where information on the I-131 ground deposition density is unknown [7].

For this purpose, the investigations of correlation between I-129 and I-131 deposition densities are very important. This pilot study aimed to investigate the correlations between I-129 ground deposition densities measured in 2000 and those of I-131 measured in 1986.

2. Material and methods

Field missions were performed by the joint team of specialists from Medical Radiological Research Center of Russian Academy of Medical Sciences (MRRC RAMS) (Russia), Gomel branch of Institute of Radiation Medicine (IRM) (Belarus), Hiroshima University (Japan). Additional personnel from MRRC RAMS and Gomel branch of IRM supported the field missions.

Soil samples were collected and I-129, Cs-137 ground deposition densities were measured in the three contaminated raions of Belorussia (total 14 locations in 12 settlements — see Results).

The spectrometric measurements of I-131 and Cs-137 activity in soil and grass samples were performed during the very first weeks after the Chernobyl accident in 1986 [5] in the vicinity of 10 out of 12 settlements, which were investigated in this study. The exact positions of sampling locations are now unknown, but in any case it is a good occasion to compare our estimates with the year 1986, which were obtained in the vicinity of the same settlements.

The following equipment was used during field missions:

- Mobile spectrometry Lab on the base of microbus;
- GPS system;

- Special soil samplers;
- Dose rate meters;
- Electro Power generator; and
- Photo and video cameras for documentations.

I-129 measurements in soil samples were performed as follows:

- Rapid desiccation and crushing of big quantity of the soil by special oven and crusher (20 kg/h up to 1-mm soil grains);
- Iodine separation and absorption (provides separation of Cs-137 and Sr-90 from iodine, as well) — Iodine removed from absorption element to liquid solution;
- Preparation of optically clear sample with liquid scintillator; and
- Registration of I-129 decays by beta-x coincidence system with MDA for I-129 as 0.002 Bq/sample.

It was assumed that the value of ratio I-131/I-129 near the Chernobyl NPP (Unit No. 4) at the time of the accident was 4×10^7 with standard deviation of 14% [8].

On this base, the ratios of I-129/Cs-137, which were estimated on the base of measurements in sampling points, were recalculated to the values of I-131/Cs-137. Cs-137 contamination data were adapted in 1986.

3. Results

Results of I-129 and Cs-137 measurements in soil samples from different locations are presented in Table 1.

Table 1
Ground deposition density of I-129 and Cs-137 measured in 2000

Settlements	Cs-137 (kBq/m^2) (11%)[a]	I-129 (Bq/m^2) (26%)[a]
Kryuki	16000	3.3
Masani	8800	9.2
Ulasi	4400	1.6
Bartolomeevka	2400	0.67
Strelichevo	1200	0.73
Dvorische-2	940	0.86
Dvorische-1	920	0.77
Novoselki	600	0.29
Pirki	570	0.11
Vit	480	0.57
Marino	410	0.22
Klivi	340	0.70
Velikiy Bor-2	190	0.17
Velikiy Bor-1	73	0.11

[a] Coefficient of variation (CV).

Table 2
Comparison of I-131/Cs-137 ratios obtained by the present work and by direct measurement in 1986

Settlements	I-131/Cs-137 ratio by the present work[a] (31%)[b]	I-131/Cs-137 ratio by direct measurement in 1986			
		Min[c]	Mean[c]	Max[c]	Number of locations in the vicinity[c]
Kryuki	8.2	7.6	16	37	11
Masani	42	12	15	26	3
Ulasi	14	8.1	14	49	7
Bartolomeevka	11	3.8	6	7.9	3
Strelichevo	24	15	18	26	4
Dvorische	35	7.1	15	29	3
Novoselki	19	12	15	17	6
Pirki	7.7	4.5	9	24	7
Vit	48	–	23	–	1
Veliky Bor	48	16	18	21	4

[a] Reconstructed by the measurements of I-129 and Cs-137 in 2000.
[b] Coefficient of variation (CV).
[c] Data from [5].

Table 2 and Fig. 1 present the results of comparison of I-131/Cs-137 ratios, which are based on the measurements in the soil samples of I-129 and Cs-137 activity in 2000, with these ratios, based on the direct I-131 and Cs-137 measurements in 1986 in the same settlements.

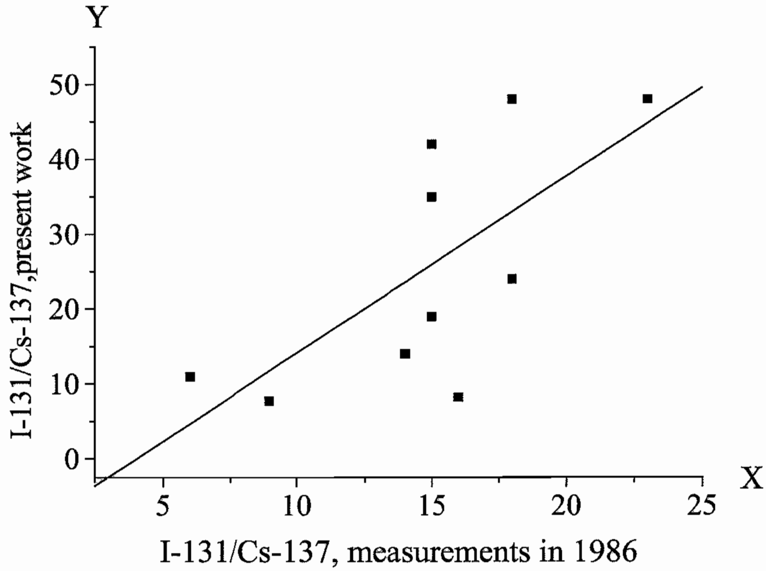

Fig. 1. Comparison of I-131/Cs-137 ratios based on the measurements of I-129 and Cs-137 activity in the soil samples in the year 2000 (denoted by *Y*) with those (denoted by *X*) based on the direct measurements of I-131 and Cs-137 in 1986 [5]: both measurements were conducted in the same settlements. Each square point denotes the value of I-131/Cs-137 (*X*) and the mean value of I-131/Cs-137 (*Y*) for the 10 respective settlements (Table 2). The solid line depicts the regression line given by Eq. (1) in Discussion.

4. Discussion

The following regression was estimated based on the data shown in Table 2 (see Fig. 1 as well).

Dependence of the ratio I-131/Cs-137 (present work denoted by *Y*) on the ratio I-131/Cs-137 (according to the measurements in 1986 denoted by *X*) is:

$$Y = -9.52(\pm 13.7) + 2.36(\pm 0.88)X \quad (1)$$

Coefficient of correlation in Eq. (1) is R=0.69. The regression coefficient in Eq. (1) has a value larger than "1" (2.36±one standard deviation 0.88).

One of the possible explanations of this result—its accumulation of long-lived I-129 fallout in the soil in comparison with short-lived I-131.

Further work in this direction (more measurements and more statistics) and comparisons with other methods are desirable (comparison with mass spectrometry methods are in process now).

5. Conclusion

Comparisons of I-131/Cs-137 ratios, which were reconstructed on the basis of I-129 measurements in 2000, with I-131/Cs-137 ratios obtained by direct measurements in 1986, showed good agreement: correlation coefficient is equal to 0.69 and linear regression coefficient is equal to 2.36 (±one standard deviation 0.88). The study confirms the possibility to apply the data on I-129 ground deposition densities for further application to improve thyroid absorbed doses estimations, which result from Iodine-31 irradiation.

Acknowledgements

The authors wish to thank Sasakawa Memorial Health Foundation for providing the support of this pilot study.

References

[1] V.S. Kazakov, E.P. Demedchik, L.N. Astakhova, Thyroid cancer after Chernobyl, Nature 21 (1992) 359.
[2] I.A. Likhtarev, B.G. Sobolev, I.A. Kairo, N.D. Tronko, T.I. Bogdanova, V.A. Oleinic, E.V. Epshtein, V. Beral, Thyroid cancer in the Ukraine, Nature 365 (1995) 375.
[3] A.F. Tsyb, E.M. Parshkov, V.V. Shakhtarin, V.F. Stepanenko, V.G. Skvortsov, I.V. Chebotareva, Thyroid cancer in children and adolescents of Bryansk and Kaluga regions, in: A. Karaoglou, G. Desmet, G.N. Kelly, H.G. Menzel, (Eds.), The Radiological Consequences of the Chernobyl Accident, Proceedings of the First International Conference (Minsk, Belarus, 18–22 March 1996), Luxembourg: European Commission and the Belarus, Russian and Ukrainian Ministries on Chernobyl Affairs, Emergency Situation and Health, EUR 16544 EN, 1996, pp. 691–698.
[4] Yu.I. Gavrilin, V.T. Khrouch, S.M. Shinkarev, N.A. Krysenko, A.M. Skryabin, A. Bouville, L.R. Anspaugh, Chernobyl accident: reconstruction of thyroid dose for inhabitants of the Republic of Belarus, Health Phys. 76 (2) (1999) 105–119.

[5] Yu.V. Dubina, Yu.K. Shchekin, L.I. Guskina, Systematisation and Verification of the Results of Spectrometric Measurements of Soil, Grass, Milk and Milk Production Samples with the Determined ^{131}I Content, Institute of Nuclear Energy of the Belorussian Academy of Science, Minsk, 1990 (in Russian).
[6] T. Straume, A.A. Marchetti, L.R. Anspaugh, V.T. Khrouch, Yu.A. Gavrilin, S.M. Shinkarev, V.V. Drozdovich, A.V. Ulanovsky, S.V. Korneev, S.V. Brekeshev, E.S. Leonov, G. Voight, S.V. Panchenko, V.F. Minenko, The feasibility of using 129-I to reconstruct 131-I deposition from the Chernobyl reactor accident, Health Phys. 71 (1996) 1–8.
[7] V.T. Khrouch, Yu.I. Gavrilin, S.M. Shinkarev, V.F. Stepanenko, The assessment of thyroid dose due to internal exposure from ^{131}I on the basis of determination of ^{129}I content in the environments, Methodical Directions instructions MU 2.6.1.082-96. Moscow: State Committee on sanitary and epidemiological inspection of RF; Official issue, 1996 (in Russian).
[8] Yu.A. Izrael, S.M. Vakulovsky, V.A. Vetrov, V.N. Petrov, F.A. Rovinsky, E.D. Sukin, Chernobyl: Radioactive Contamination of the Environment, Hydromet Publishing House, St. Petersburg, 1990 (in Russian).

International Congress Series 1234 (2002) 121–126

A comparative study on thyroid diseases among children in Gomel region, Belarus

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Abstract

A study aimed at comparing the prevalence of thyroid diseases between children born before and after the accident was outlined with emphasis on rationale and design of the study. In the study, a total of 21 601 children in Gomel city and four districts in the neighborhood of Gomel city were examined from February 1998 to December 2000. There were 9720 children born from January 1, 1983 to April 26, 1986 (Group I), 2409 children born from April 27, 1986 to December 31, 1986 and 9472 children born from January 1, 1987 to December 31, 1989 (Group III). Out of the examined children, 32 (0.15%) thyroid cancers were found, among whom 31 were in Group I and one was in Group II, while no cases in Group III. Our findings demonstrate the likelihood that short-lived radioactive fallout due to the Chernobyl accident induced thyroid cancer in children living near Chernobyl. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Chernobyl accident; Causation; Epidemiology; Short-lived fallout; Thyroid cancer

1. Introduction

An enormous increase in childhood thyroid cancer has been reported since the Chernobyl accident [1] but the cause of such dramatic increase has been the subject of

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0531-5131/02
PII: S0531-5131(01)00602-1

controversy. The Chernobyl Sasakawa Health and Medical Cooperation Project, a 5-year health screening program, which began in May 1991 and reached completion at the end of April 1996, was the most reliable and comparable program of its kind, revealing 62 thyroid cancers in total and 37 in the Gomel region of Belarus among about 120 000 and 19 000 children, respectively [2,3]. However, the lack of reliable estimates of individual thyroid dose has hindered conclusions about the exact effect of the Chernobyl accident on the thyroid glands of children.

In contrast to radiation exposure by atomic bombing, the mode of radiation exposure received by general population is quite complicated in the case of the Chernobyl accident. In the former case, the source of radiation was in effect fixed and people received directly a high rate of external radiation instantaneously, while in the latter case, general population received external and internal radiation exposure caused by fallout. Dose estimation is a very difficult issue. Even in the case of the atomic bombing, which is quite simpler than the case of the Chernobyl accident, it took more than 40 years to reach a dosimetry system that deems most reliable: the system, however, is still under revision. Furthermore, we should note that the dosimetry system for the atomic bombing could be validated by measuring radiation activities of available exposed materials such as bricks collected in several places in Hiroshima and Nagasaki. In the case of the Chernobyl accident, however, dose estimation is totally dependent on a model whose validity is in principle impossible to prove. Even in the case in which ^{131}I specific activity at the thyroid gland was measured, individual estimate of thyroid dose varies with the model adopted.

To overcome the shortage of accurate dosimetry data, we launched a new study aimed at comparing children born before and after the accident on the basis of the hypothesis that if children's thyroid glands were affected by the accident, the prevalence of thyroid diseases, especially thyroid cancer, would be significantly and selectively higher in children born before the accident than in those born after the accident.

2. Subjects and methods

The prevalence of childhood thyroid cancer in Gomel region observed in the 5-year health examination of the Chernobyl Sasakawa Health and Medical Cooperation Project was about 1.9 per 1000 persons. We therefore estimated the number of children to be examined in the new project as enough to detect, with probability of 90% or more, a decrease in the prevalence of thyroid cancer by 1/10 in the children born after the accident as compared with those born before the accident. We assumed the prevalence of thyroid cancer in children born before the accident to be 1 per 1000 persons and calculated the sample size necessary for assuring the above-mentioned power for the statistical hypothesis test of the 5% significance level. The sample size thus calculated was 12 000 for each group.

We reviewed the population in several districts in the neighborhood of Gomel city and reached a decision, taking feasibility and other issues into account, to screen children born from January 1, 1983 to December 31, 1989 and living in Gomelskii, Hoynikskii, Loevskii and Rechitskii districts and Gomel city in the Gomel region of Belarus. These areas are within a radius of 150 km from the Chernobyl Nuclear Power Plant (Fig. 1). We conducted the health screening at all schools except Gomel city, where we sampled seven schools with an enrolment over 1000 using the stratified random sampling procedure. In effect, therefore, we examined all of the targeted children in the four districts and about 10% of those in Gomel city.

The thyroid gland examination consisted of an ultrasound examination as well as measurement of the serum thyroid-stimulating hormone and free thyroxine levels and antithyroid peroxidase antibody. Ultrasound examinations were performed with Logic α100 (7.5 MHz) equipped with a digital image recorder (GE Yokogawa Medical Systems, Tokyo). Children with thyroid ultrasonographs showing nodules of over 5 mm in diameter or abnormal echogenity further underwent echo-guided fine-needle aspiration biopsy. To reach a final diagnosis in suspected cases, the ultrasonographs, microscopic cytology of echo-guided fine-needle aspiration biopsy, results of thyroid examinations and other important information were sent to Nagasaki University School of Medicine from Gomel Specialized Medical Dispensary via the telemedicine system (developed by us and operating from February 1999) [4].

All of the data are processed in an Oracle database developed by two computer technicians of the Mogilev Regional Medical Diagnostic Center (SPG) and Gomel Specialized Medical Dispensary (VNA). Data entry has been conducted using special software that displays on the computer screen a form similar to that used for health examination.

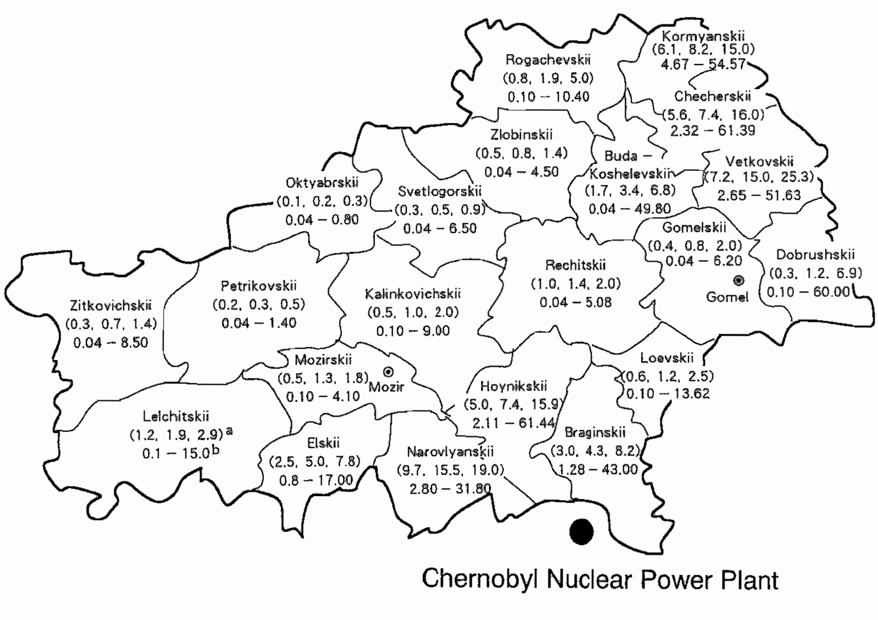

Fig. 1. Districts of the Gomel region with ^{137}Cs contamination levels (Ci/km^2) as measured in 1992. [a]The triplets give the 25th, 50th and 75th sample percentiles of contamination levels. [b]Minimum and maximum levels of contamination.

3. Results

A total of 21 601 children were examined from February 1998 to December 2000: 9720 were born from January 1, 1983 to April 26, 1986 (Group I); 2409 were born from April 27, 1986 to December 31, 1986 (Group II); and 9472 were born from January 1, 1987 to December 31, 1989 (Group III).

A total of 32 (0.15%) thyroid cancers were detected: 31 of them were in Group I (0.32%), one in Group II (0.04%) and no cases in Group III. All of the patients underwent surgery at the Thyroid Oncology Center in Minsk and were confirmed by histological diagnosis: all were cases of papillary adenocarcinoma and 13 had undergone surgery prior to screening, i.e., from October 1993 to January 1998.

A significant difference in the prevalence of thyroid cancer among the three groups is apparent, as shown in Fig. 2. However, the distribution of age at the time of the examination is different among the three groups as well. Since the age as well as the sex is a major factor to increase the risk of thyroid cancer, as shown in the upper right hand side of Fig. 3, we compared the prevalence of thyroid cancer among children aged 11–13 years. Out of 10 055 children in this age class, 2627 were in Group I, 2086 in Group II and 5342 in Group III. A significant difference in the prevalence of thyroid cancer among the three groups is also seen in the left-hand side of Fig. 3. A formal statistical analysis on the

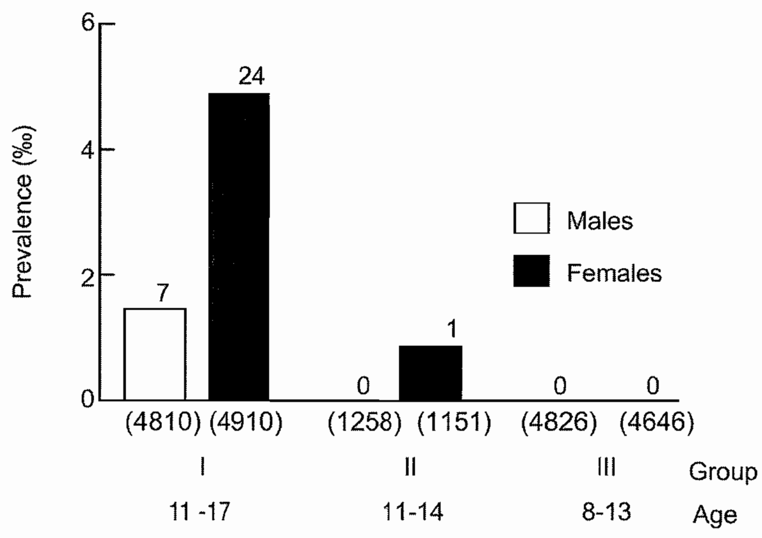

Fig. 2. Prevalence of thyroid cancer (per 1000) by sex and birth period in 21 601 children living in Gomelskii, Hoynikskii, Loevskii and Rechitskii districts and Gomel city in the Gomel region of Belarus. Examination was carried out at schools from February 1998 to December 2000. The parenthetic entry refers to the number of children examined and the figure on the bar indicates the number of cancer cases. Group I = children born from January 1, 1983 to April 26, 1986; Group II = children born from April 27, 1986 to December 31, 1986; Group III = children born from January 1, 1987 to December 31, 1989. The age (years) refers to that at the time of examination.

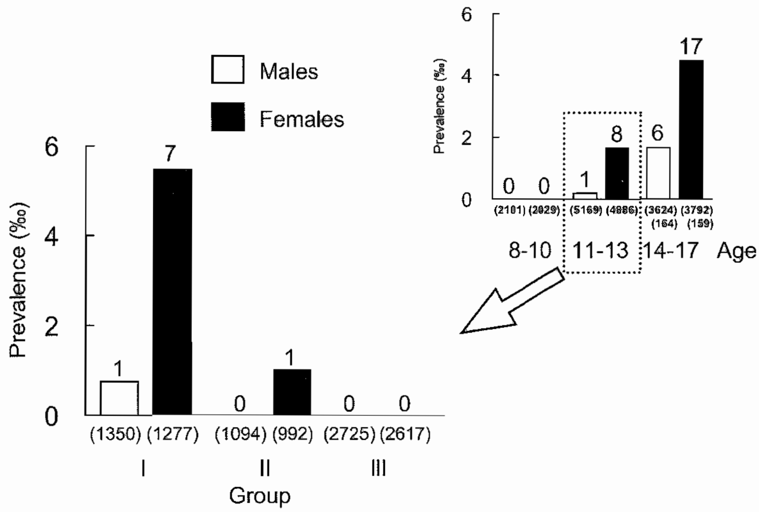

Fig. 3. Upper right hand side: prevalence of thyroid cancer (per 1000) by sex and age at the time of examination. The group of children aged 14–17 years included those in Group I and Group II; the parenthetic entry in the lower line refers to the number of children in Group II while that in the upper line refers to the total number of children in Group I or II. Left-hand side: prevalence of thyroid cancer (per 1000) by sex and age at the time of examination in children aged 11–13 years. See Fig. 2 for details.

basis of individual data demonstrated a significant ($p = 0.006$) difference in the prevalence of thyroid cancer among the three groups after adjustment for sex and age [5].

4. Discussion

Since the design of our health examination was school-based, differences in environmental factors after the accident were deemed small. The major difference in background was that the children in Group III were not exposed to fallout caused by the Chernobyl accident, while the children in Groups I and II were probably exposed to fallout directly or in utero, respectively.

Our findings demonstrate the likelihood that thyroid cancers detected in children after the Chernobyl accident were caused by direct external or internal exposure to short-lived radioactive fallout including ^{131}I and ^{133}I. People exposed to the Chernobyl accident in their childhood are at high risk for thyroid cancer, and establishment of a global support system to provide careful and continuous follow-up is urgently needed.

Acknowledgements

The authors thank Dr. Vladimir S. Vorobey (Chief Physician, Gomel Specialized Medical Dispensary) and Dr. Tadeush A. Kroupnik (Chief Physician, Mogilev Regional Medical Diagnostic Center) for their cooperation in carrying out the project. We express our special thanks to Dr. Itsuzo Shigematsu, Prof. Kenzo Kiikuni and Dr. Shigenobu Nagataki (Sasakawa Chernobyl Scientific Committee) for their support and encouragement without which the present study would not have been realized.

References

[1] V.S. Kazakov, E.P. Demidchik, L.N. Astakova, Thyroid cancer after Chernobyl, Nature 359 (1992) 21.
[2] S. Yamashita, Y. Shibata (Eds.), Chernobyl: A Decade, Elsevier, Amsterdam, 1997.
[3] S. Yamashita, M. Ito, K. Ashizawa, Y. Shibata, S. Nagataki, K. Kiikuni, Monitoring and prevention of the thyroid carcinoma in a population exposed to radiation, in: G. Thomas, A. Karaoglou, E.D. Williams (Eds.), Radiation and Thyroid Cancer, World Scientific, Singapore, 1999, pp. 369–376.
[4] S. Yamashita, Y. Shibata, N. Takamura, K. Ashizawa, N. Sera, K. Eguchi, Satellite communication and medical assistance for thyroid disease diagnosis from Nagasaki to Chernobyl, Thyroid 9 (1999) 969.
[5] Y. Shibata, S. Yamashita, V.B. Masyakin, G.D. Panasyuk, S. Nagataki, 15 years after Chernobyl: new evidence of thyroid cancer, Lancet 358 (2001) 1965–1966.

International Congress Series 1234 (2002) 127–134

Post Chernobyl NIS thyroid tissue, nucleic acid and data banks and integrated research

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Abstract

The increased incidence of thyroid carcinoma in patients, resident in the contaminated areas of Belarus, Ukraine and Russia and who were aged under 19 at the time of the Chernobyl accident has provided a unique opportunity for the scientific study of a human tumour of known radiation aetiology. It is important that not only the interests of the patients concerned come first, but also that information is not lost that may inform our response to a future accident, or could improve prognosis for those affected. We have therefore set up the first international cooperation — the Newly Independent States Chernobyl Tissue Bank (known by the acronym NISCTB) — that makes available a collection of biological samples from tumours and normal tissues from these patients. Full ethical permission is obtained for each sample and the project is carried out with the agreements of the governments of Belarus, Ukraine and Russia. A full description of the specimen; its location within the thyroid; whether other tumours are present in the gland and the relative locations of material from which RNA and DNA is extracted after frozen section confirmation, together with an internationally agreed diagnosis is recorded on the project database. The database also contains anonymised basic clinical information on each patient donating material to the project. Researchers who obtain material from the NISCTB agree to provide their results to the Coordinating Centre on a case by case basis on completion of their project. We hope that this project will become a paradigm for investigations on the mechanisms of human cancer, and provide a basis that fosters international collaboration in thyroid research.

Keywords: Chernobyl; Thyroid cancer; Tissue resource

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PII: S0531-5131(01)00603-3

1. Introduction

Thyroid cancer in children and young people is usually extremely rare (of the order of 1–1.5 per million cases per year for those under 15 years of age at operation). However, in the areas of Belarus, Ukraine and Russia that were contaminated by fallout from the nuclear disaster at the Chernobyl Power Plant in 1986, there has been a very large increase in thyroid cancer in those who were exposed to fallout as children. This is highest in those areas which received the highest levels of radioiodine contamination. The largest increase in incidence has been in Gomel oblast in Southern Belarus (90 per million per year for those under 15 at operation). To date, there have been approximately 1800 cases of thyroid cancer in children and young adults in Belarus, Northern Ukraine and in those areas of Russia contaminated by fallout. So far, the increase in thyroid cancer is the only unequivocal carcinogenic consequence of exposure to radioactive fallout from the accident.

There are two main types of thyroid cancers that derive from the thyroid follicular cell; papillary carcinoma and follicular carcinoma. Although the separation of these two types was initially based on morphology, it is now clear that the two types exhibit different clinical behaviour and are associated with different molecular biological profiles. Papillary carcinomas are more frequently associated with rearrangement of the ret and trk oncogenes [1,2] and follicular carcinoma with mutation in one of the ras oncogenes [3]. The increase in thyroid cancer post Chernobyl has been largely restricted to papillary carcinoma [4–6] and in particular to a particular subtype, which is associated with a particular rearrangement of the ret oncogene [7–9]. Despite the conclusions of the first small studies on the molecular biology of post Chernobyl papillary carcinomas [10,11], it now appears that the frequency of ret involvement in these tumours is not significantly different from that in a control, non-irradiated population [12,13]. Mutations in other genes known to be associated with thyroid carcinogenesis such as trk, the TSH receptor, the ras oncogenes and p53 have not been identified in a significant proportion of post Chernobyl thyroid carcinomas [9,14–16]. Despite all the scientific studies on thyroid carcinoma, whether related to Chernobyl or not, there is still much to discover about both the prognosis of thyroid cancer and the development of new therapeutic areas. While thyroid cancer, and papillary carcinoma in particular, is not associated with a high mortality rate when compared with other cancers, it is still important to carry out research which may lead to earlier diagnosis or the ability to define those who may be at increased risk for the development of thyroid cancer, both in general and in particular following exposure to radiation.

The occurrence of such a large number of human tumours of a single tissue, the majority of which are of a single histological type, due to a known cause at a known time provides an opportunity to fully investigate the link between exposure to radiation and thyroid carcinogenesis. This is a unique situation that demands a unique response. In order to meet this need a cooperative project (known by the acronym NISCTB, for Newly Independent States Chernobyl Tissue Bank) between the governments of Belarus, Russia and Ukraine and the European Commission (EC), the National Cancer Institute (NCI) of the USA, the Sasakawa Memorial Health Foundation (SMHF) of Japan and the World Health Organisation (WHO) has been established. The project seeks to provide material that has been obtained and documented in a uniform manner, to scientists investigating mechanisms that underlie the development of thyroid neoplasia following exposure to fallout from Chernobyl. It is hoped that the results from the studies that use this valuable resource will lead in the future to better patient care and prognosis through an increased understanding of the factors that have led to tumour development. The project is governed by five important principles.

- The interests of the patient must come first.
- Spare tissue of potential value must not be wasted.
- Blood and tissue samples should only be used if appropriate consent is given by the patient and the appropriate laws of the country are observed.
- A tissue bank should be established in the country in which the tissue was removed.
- International agencies should participate in the project providing financial support, training, equipment and expert advice.

2. Management of the project

The responsibility for the project as a whole is taken by the Collaborative Management Committee and all Panels report to this committee, either directly or through the Scientific Project Panel. The Collaborative Management Committee is comprised of one representative of each of the funding organizations (the EC, the NCI of the US, the SMHF of Japan and the WHO) and of the Ministries of Health of Belarus, Ukraine and Russia, and is responsible for overseeing political and financial matters relating to the project. The Scientific Project Panel is responsible for overseeing scientific issues related to the project and is composed of two scientists nominated by each of the funding organisations and by each of the three NIS countries concerned.

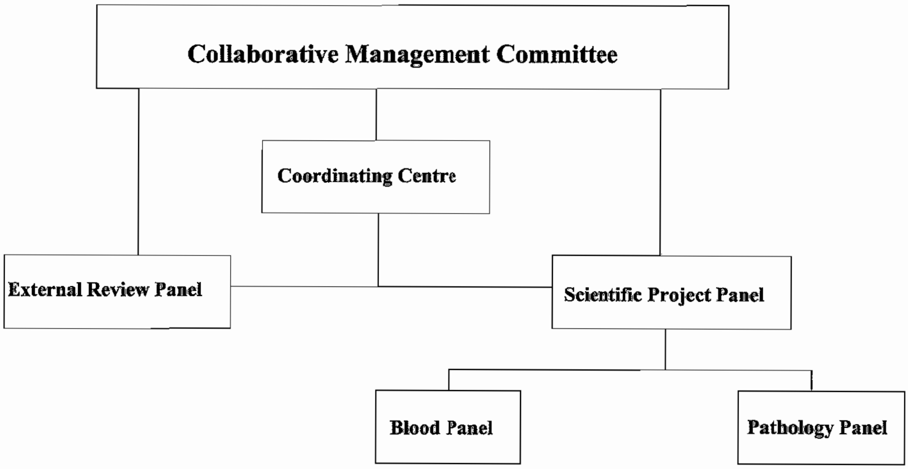

Fig. 1. Management structure of the NISCTB.

A group of experts in thyroid pathology (representing the EC, the US, Japan, Belarus, Ukraine and Russia) comprises the Pathology Review Panel that is responsible for provision of a consensus diagnosis on each specimen entered into the NISCTB. There are two additional panels; one of which provides information that relates specifically to issues concerned with blood samples. The second panel, the External Review Panel, is composed of internationally respected experts in thyroid and radiation-related research, and is responsible for reviewing applications for access by researchers for information and material from the NISCTB, i.e., a peer review group. The entire project is coordinated from the University of Cambridge (UK). The relationship between the Coordinating Centre in Cambridge and the various panels is shown in the diagram (see Fig. 1).

3. Scope of the project

3.1. Study cohort

The project collects material from post operative specimens of thyroid carcinoma and cellular adenoma from patients who were born after 26th April 1967 (i.e., who were aged under 19 at the time of the Chernobyl accident) and who are or were at the time of the accident, resident in Belarus, the northern oblasts of Ukraine, or the four contaminated oblasts of Russia. Thyroid cancer is extremely rare in this age group; we can therefore be reasonably sure that the majority of cases are as a result of exposure to radioiodine in fallout from Chernobyl, particularly in those diagnosed and operated on in childhood and adolescence.

3.2. Aims of the project

The aims of the project are to provide

- aliquots of RNA and DNA extracted from tumour and normal thyroid tissue, together with aliquots of DNA and serum from blood for research;
- an internationally agreed pathology diagnosis for each specimen for patient diagnosis and research;
- complete documentation of the specimen;
- information on sex, age at exposure and operation, oblast of residence;
- an agreed mechanism of access to materials and information for established research groups;
- a database which records not only all the information about the specimens held in the bank but also the results of studies using material from the bank on a case by case basis to permit later correlation of multiple oncogene involvement in the same tumour.

The NISCTB commenced collection of material from post operative thyroid specimens and documentation of the pathology of these specimens on 1st October 1998. Collection of blood samples commenced in 2000. There is a defined protocol for documentation and storage for each type of specimen that has been agreed by the doctors responsible for day to day management of the patients in the three NIS Institutes.

3.3. Collection of material

Informed consent is obtained from the patient or his/her parent or guardian, a sample of blood is taken pre-operatively for serum separation and extraction of DNA from blood. The patient is then operated and the operative specimen is seen by the pathologist. The location of the tumour or tumours is recorded on a simple diagram that is later scanned into the project database. The positions from which blocks of tissue that will be processed to paraffin for diagnosis are taken are marked on the diagram. When the pathologist has taken the material that is necessary for accurate diagnosis, small blocks of tissue from the remainder of the tumour and normal thyroid are taken and snap frozen. The majority of these tumours are small, but where possible three blocks of tissue from tumour and three from normal thyroid are taken. The positions of these blocks relative to those taken for paraffin are noted on the form.

A frozen section of each block of tissue is taken for future entry into the database using a digital camera attached to a microscope. Each piece of tissue is stored in its own cryotube at −70 °C; each tube is labelled with a unique coded number. Paraffin sections of each case are supplied to the six monthly meetings of the International Pathology Panel, which includes expert thyroid pathologists from the EC, the US and Japan as well as a representative each from Belarus, Russia and Ukraine, for provision of a consensus diagnosis.

It is very important to ensure that all the information relating to these specimens is stored in a way that can be accessed easily. Each of the three Institutes involved in the project (Research and Clinical Institute for Radiation Medicine and Endocrinology in Minsk, the Institute of Endocrinology and Metabolism in Kiev, and the Medical Radiological Research Centre of the Russian Academy of Sciences in Obninsk) has been provided with a specially designed Access database. The database has an identical format in each of the three Institutes and a back-up integrated database is kept at the Coordinating Centre at the University of Cambridge in England. All patient data is anonymised and is totally confidential. The identical format enables regular updates to be made to the Coordinating Centre and facilitates exchange of data between centres. The database records not only the minimum dataset — date of operation, date of birth, sex, oblast of residence, and the pathology panel diagnosis — but also information related to the number and location of frozen tissue samples, aliquots of nucleic acid, blood samples, serum and those researchers to whom material and information has been issued.

One of the major aims of the project is the release of DNA and RNA from tissue sample and DNA from blood to researchers. Provision of pieces of tissue to individual researchers would result in considerable wastage of nucleic acid. DNA and RNA from the same piece of tumour or normal thyroid is extracted, and the NISCTB provides aliquots of nucleic acid to researchers. The standard size for these aliquots is 5 μg. The nucleic acids are extracted to an internationally agreed protocol; currently, this is being done by scientists from the Eastern institutes working in Western laboratories, but this will be carried out in the Eastern institutes by the end of 2001. Quality control is carried out on each extract by reverse transcriptase polymerase chain reaction (RT-PCR) for RNA and PCR for DNA. The quality control information is recorded on the database and provided to researchers using the material. Aliquots of DNA from blood will be available by Autumn 2001.

We have currently documented 947 cases of thyroid carcinoma and adenoma from patients aged under 19 at the Chernobyl accident and operated since 1st October 1998. The majority of these cases are papillary carcinoma. Frozen material has been collected from 747 of these cases; in the majority of cases, paired samples of tumour and normal tissue are available and the presence of tumour is confirmed by frozen section of the tissue block prior to extraction of nucleic acids. Aliquots of DNA and RNA area available from 292 cases; this number will almost double by Autumn 2001. In total, there are more than 3000 aliquots of RNA and DNA from normal thyroid and thyroid tumours. In the majority of cases, multiple aliquots are available from each case; this will permit multiple analyses to be performed by different laboratories on the same piece of tumour/normal tissue. In addition, samples of serum and DNA from blood are or will shortly be available from 177 of these cases.

4. Access to information and material from the NISCTB

Applications for access to materials from the NISCTB are now invited from the worldwide scientific community. It is important that distribution of the material is seen as fair. The applications are reviewed by an independent external panel of experts, nominated by the three governments and four sponsors. There is no deadline for submissions of applications for access to the material, but applications are reviewed twice a year in February and August. An additional innovation in the organisation of the tumour bank is that researchers who obtain material from the resource agree to provide the results of their investigations to the NIS Institutes involved via the Coordinating Centre on a case by case basis. This information will not be used until after the researchers have published their findings, but it will allow the results of all of the studies to be correlated at a later date, so that, for example, the investigations by different groups of a number of different genes can be correlated to study their interactions. The provision of extracted nucleic acid from thyroid tissue, rather than each researcher being provided with a small piece of tissue, maximises the amount of data that can potentially be obtained from a single operative specimen and will enable multiple molecular biological studies to be carried out for each case. It is already clear that it is likely to be the interaction of suites of genes which is responsible for both susceptibility to development of human cancer and the biological mechanisms which influence tumour growth. In addition, the approach that we have taken will permit multiple analysis on individual samples from the same piece of tumour and compare these with analysis on a separate area of tumour. This will enable scientists to investigate the heterogeneity of a given tumour — a factor that may prove very important in the future design of therapeutic strategies. The NISCTB aims to provide material for study not only by this generation of scientists but also the next generation, which may be in a position to benefit from a much more detailed analysis.

Further information about the project and full details on the application process are available on the project website (http://www.srl.cam.ac.uk/nistcb). The first group of applications were reviewed and approved in June 2001. The NISCTB actively encourages cooperation, whenever possible, between the NIS Institutes involved in the collection of material for the NISCTB and researchers based outside Belarus, Ukraine and Russia. It also hopes to be able to offer a number of fellowships to NIS participants to collaborate in research projects receiving material from the NISCTB in the near future.

This is truly a cooperative project and if it were not for the dedication of many scientists based in the three NIS Institutes involved in the project, and the political goodwill of the governments of Belarus, Ukraine and Russia, this unique response to a unique situation could not have been brought to fruition. We hope that this project will become a paradigm for investigations on the aetiology of human cancer, and will provide a basis that reduces the chance of competition and even friction between groups in their requests for this limited resource, and will foster international collaboration.

Acknowledgements

Financial support from the following is gratefully acknowledged: European Commission, the National Cancer Institute of the USA, the Sasakawa Memorial Health Foundation of Japan and the World Health Organisation. In addition, we acknowledge the support of the governments of Belarus, Ukraine and Russia together with all of the scientists who comprise the various panels which oversee the project, too numerous to mention individually, but without them this project could not have succeeded.

References

[1] M. Santoro, F. Carlomango, I.D. Hay, Ret oncogene activation in human thyroid neoplasms is restricted to the papillary cancer subtype, J. Clin. Invest. 89 (1999) 1517–1522.

[2] A. Grieco, M.A. Pierotti, I. Bongarzone, J. Pagliardini, C. Lanzi, G. Della Porta, Trk-T1 is a novel oncogene formed by the fusion of TPR and Trk genes in human papillary cancer, Oncogene 7 (1992) 237–242.

[3] N.R. Lemoine, E.S. Mayall, F.S. Wyllie, E.D. Williams, M. Goyns, B.M.J. Stringer, D. Wynford-Thomas, High frequency of ras oncogene activation in all stages of human thyroid tumourigenesis, Oncogene 2 (1989) 159–164.

[4] T. Bogdanova, M. Bragarnik, N.D. Tronko, H.R. Harach, G.A. Thomas, E.D. Williams, The pathology of thyroid cancer in Ukraine post Chernobyl, in: A. Karaoglou, D. Desmet, G.N. Kelly, H.G. Menzel (Eds.), The Radiological Consequences of the Chernobyl Accident, European Commission EUR 16544 EN, 1996, pp. 785–789.

[5] E. Cherstvoy, V. Pozcharskaya, H.R. Harach, G.A. Thomas, E.D. Williams, The pathology of childhood thyroid carcinoma in Belarus, in: A. Karaoglou, G. Desmet, G.N. Kelly, H.G. Menzel (Eds.), The Radiological Consequences of the Chernobyl Accident, European Commission EUR 16544 EN, 1996, pp. 779–784.

[6] A.Y. Abrosimov, E.F. Lushnikov, A.F. Tsyb, H.R. Harach, G.A. Thomas, E.D. Williams, The pathology of childhood thyroid tumours in the Russian Federation after Chernobyl, in: A. Karaoglou, G. Desmet, G.N. Kelly, H.G. Menzel (Eds.), The Radiological Consequences of the Chernobyl Accident, European Commission EUR 16544 EN, 1996, pp. 791–793.

[7] Y.E. Nikiforov, J.M. Rowland, K.E. Bove, H. Monforte-Munoz, J.A. Fagin, Distinct pattern of ret oncogene rearrangements in morphological variants of radiation-induced and sporadic thyroid papillary carcinomas in children, Cancer Res. 57 (1997) 1690–1694.

[8] G.A. Thomas, H. Bunnell, H.A. Cook, E.D. Williams, A. Nerovnya, E.D. Cherstvoy, M.D. Tronko, T.I.

Bogdanova, G. Chiapetta, G. Viglietto, F. Pentimalli, G. Salvatore, A. Fusco, M. Santoro, G. Vecchio, High prevalence of RET/PTC rearrangements in Ukrainian and Belarussian post Chernobyl thyroid papillary carcinomas: a strong correlation between RET/PTC3 and the solid/follicular variant, J. Clin. Endocrinol. Metab. 84 (1999) 4232–4238.

[9] M. Santoro, G.A. Thomas, G. Vecchio, G.H. Williams, A. Fusco, G. Chiappetta, V. Pozcharskaya, T.I. Bogdanova, E.D. Cherstvoy, L. Voscoboinik, M.D. Tronko, A. Carss, H. Bunnell, M. Tonnachera, J. Parma, J.E. Dumont, G. Keller, H. Höfler, E.D. Williams, Gene rearrangement and Chernobyl related thyroid cancers, Br. J. Cancer 82 (2000) 315–322.

[10] S. Klugbauer, E. Lengfelder, E.P. Demidchik, H.M. Rabes, High prevalence of ret rearrangement in thyroid tumors of children from Belarus after the Chernobyl reactor accident, Oncogene 11 (1995) 2459–2467.

[11] L. Fuggazzola, S. Pilotti, A. Pinchera, T.V. Vorontsova, P. Mondellini, I. Bongarzone, A. Greco, L. Astakhova, M.G. Butti, E.P. Demidchik, F. Pacini, M.A. Pierotti, Oncogenic rearrangements of the ret protooncogene in papillary thyroid carcinomas from children exposed to the Chernobyl nuclear accident, Cancer Res. 55 (1995) 5617–5620.

[12] G.H. Williams, S. Rooney, G.A. Thomas, G. Cummins, E.D. Williams, Ret activation in adult and childhood papillary thyroid carcinoma using a RT-nPCR approach on archival material, Br. J. Cancer 74 (1996) 585–589.

[13] J. Smida, K. Salassidisk, L. Hieber, H. Zitzelsberger, A.M. Kellerer, E.P. Demidchik, T. Negele, F. Spelsberg, E. Lengfelder, M. Weiner, M. Bauchinger, Distinct frequency of ret rearrangements in papillary thyroid carcinomas of children and adults from Belarus, Int. J. Cancer 80 (1999) 32–38.

[14] C. Beimfohr, S. Klugbauer, E.P. Demidchik, E. Lengfelder, H.M. Rabes, NTRK1 rearrangement in papillary thyroid carcinomas of children after the Chernobyl reactor accident, Int. J. Cancer 80 (1999) 842–847.

[15] B. Suchy, V. Waldmann, S. Klugbauer, H.M. Rabes, Absence of RAS and p53 mutations in thyroid carcinomas of children after Chernobyl in contrast to adult thyroid tumours, Br. J. Cancer 77 (1998) 952–955.

[16] J. Smida, H. Zitzelsberger, A.M. Kellerer, L. Lehmann, G. Minkus, T. Negele, F. Spelsberg, L. Hieber, E.P. Demidchik, E. Lengfelder, M. Bauchinger, p53 mutations in childhood thyroid tumours from Belarus and in thyroid tumours without radiation history, Int. J. Cancer 73 (1997) 802–807.

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The World Health Organization and Sasakawa Memorial Health Foundation joint project: medical relief for children affected by the Chernobyl accident through the development and implementation of health telematics

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Abstract

The World Health Organization (WHO) and Sasakawa Memorial Health Foundation (SMFH), in cooperation with the Ministry of Health of the Republic of Belarus (the Ministry), have established and promoted a project entitled "Medical Relief for Children Affected by the Chernobyl Accident through the Development and Implementation of Health Telematics" to improve early diagnosis of thyroid diseases and follow-up of patients who have developed thyroid cancer due to exposure to radioactive fallout. The article reviews the development and current status of the project. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Chernobyl; Telemedicine; Health telematics; Thyroid cancer

1. Introduction

The World Health Assembly, in its Resolution 49.22 (25 May 1996), urged Member States to participate actively in, and to provide further support, for the implementation of the International Programme to mitigate the Health Effects of the Chernobyl Accident. It has also requested the Director-General to give emphasis to the monitoring and mitigation

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PII: S0531-5131(01)00604-5

of long-term health effects in highly exposed groups including children. In 1999, following this resolution, the World Health Organization (WHO) and the Sasakawa Memorial Health Foundation (SMHF), in cooperation with the Ministry of Health of the Republic of Belarus (the Ministry), have established a project called “Medical Relief for Children Affected by the Chernobyl Accident through the Development and Implementation of Health Telematics”.

2. Background of the project

WHO and SMHF have been carrying out a number of projects aimed at humanitarian assistance in Belarus, Russia and the Ukraine, the countries most affected by the Chernobyl accident, to alleviate the medical consequences of this disaster. Medical examinations in the three countries since 1991 on about 210 000 children were performed within the framework of the WHO International Programme on the Health Effects of the Chernobyl Accident (IPHECA) and the Chernobyl Sasakawa Project. These examinations have shown a significant increase in the incidence of childhood thyroid diseases including thyroid cancer. It is particularly evident in the Gomel region, Belarus, where thyroid cancer incidence is 100 times higher than before the accident [1,2].

Analysis of the health care system at the time of the Chernobyl accident, especially in Belarus, has shown that there are still many gaps and unresolved problems. For example, there was an uneven geographical distribution of health care resources throughout the country, including facilities and manpower; inadequate access to health care in the radionuclide-contaminated areas because of remoteness of many residents from medical centres; inadequacy of modern communication facilities between primary, regional and national health care facilities; insufficient possibilities for training and education of local medical staff; and lack of information about new methods in medical practice, in particular, at the primary health care level.

WHO and SMHF considered that one of the important tasks in the continuation of humanitarian assistance to countries affected by the Chernobyl accident is the strengthening of medical care facilities, mainly in the areas most radio-contaminated and with the largest number of childhood thyroid cancer patients. In this context, both organizations were willing to initiate a project in order to improve diagnosis of thyroid diseases and follow-up of patients treated for thyroid cancer. It was decided to follow the recommendations of the WHO Group Consultation on Health Telematics Policy in support of the renewed Health-for-All Strategy in the 21st century, which was held in Geneva in 1997. According to WHO, “health telematics is a composite term for health-related activities, services and systems, carried out at distance by means of information and communication technologies, for the purposes of global health promotion, disease control and health care, as well as education, management, and research for health.” Considering health telematics opportunities for health care systems and taking into account the recommendation of the WHO Group Consultation to “Explore and promote the best use of health telematics in public health: e.g. in disease surveillance, prevention and control, health education, health promotion, health systems and service development, . . .environmental health, with particular attention to . . .specific population groups that are most in need or undeserved”, WHO and SMHF, after consultation with the Ministry, agreed to combine their efforts in the development of health telematics in Belarus focusing its implementation on the improvement of humanitarian medical relief actions for children affected by the Chernobyl accident. The idea to establish the health telematics project was supported by the positive outcome of the earlier Second Chernobyl Sasakawa Project resulting in the introduction of a telecommunication system between Gomel Specialized Medical Dispensary, Belarus, and the Nagasaki University School of Medicine, Japan [3]. Since the establishment of this system, ultrasound and cytological images of the thyroid of 448 patients, who were suspected of having thyroid abnormalities, have been sent via the Immarsat B satellite communication system from Gomel to Nagasaki [4]. It helped to diagnose thyroid cancer at early stage in 18 patients.

The current WHO–SMHF project on health telematics is a logical continuation of the Second Chernobyl Sasakawa project and is aimed at further strengthening of diagnostic capabilities of childhood thyroid cancer in Belarus through the implementation of health telematics. The WHO–SMHF project is focusing on the use of the internet for imaging information exchange. The project duration is to be 10 years with any extension to be agreed upon by the parties concerned. Funds for the initial stage of 3 years, in the amount of US$1 000 000 are available to WHO from the Sasakawa Health Trust Fund. Continuation of funding by the Sasakawa Health Trust Fund beyond the initial 3-year stage will be subject to a separate agreement between the parties. The future extension of this project to Russia and Ukraine may also be considered.

3. Main project objectives and activities

The project includes two main parts. The first is related to the improvement of early diagnosis of thyroid pathology and is called as "telepathology". The second part deals with the strengthening of education and training of medical doctors and students in Belarus, in particular to those who are working or will work in contaminated territories. This part of the project is called "tele-education".

The following short-term objectives of the project have been identified for its 3-year pilot phase:

- To improve early diagnosis and treatment of children affected by the Chernobyl accident.
- To establish the telecommunication infrastructure, including local and international network systems, which will facilitate the development of remote-area medical consultations.
- To develop remote-area assistance by establishing health telematics communication between the Gomel Specialized Dispensary and the WHO Collaborating Centre for Research on Thyroid Diseases and the Nagasaki University School of Medicine, Japan.
- To develop telematic communication links between Gomel and Minsk medical centres in order to improve the quality of diagnosis of persons exposed to radiation on the basis of better exchange of medical information within and outside Belarus.

- To develop telepathology as an integral part of the diagnostic process and follow-up of children with thyroid diseases and establish a project clinical database.
- To establish an information centre for the exchange of experience and promotion of the training and education of medical staff in Minsk and the Gomel region in the field of radiation-related thyroid pathology.

The long-term objective of the project is to establish an international telepathology network involving the medical facilities in territories contaminated by radionuclides in Belarus and relevant WHO collaborating centres, and to establish a long-term follow-up system for patients after completion of their thyroid cancer treatment.

In order to achieve the short-term and long-term objectives, WHO and the Ministry experts in collaboration with specialists from SMHF outlined the main project activities, which include the study of the local telecommunication infrastructure in Belarus for the implementation of telepathology and tele-education, supply of relevant equipment to participating institutions, development of project protocols for telepathology and tele-education, relevant training programmes, and a software for analysis of the project database.

It is planned that due to implementing project activities during the pilot phase, the health telematics infrastructure will be established in Belarus. It will facilitate communication links between Belarussian participants of the project and relevant WHO collaborating centres experienced in early diagnosis of thyroid cancer.

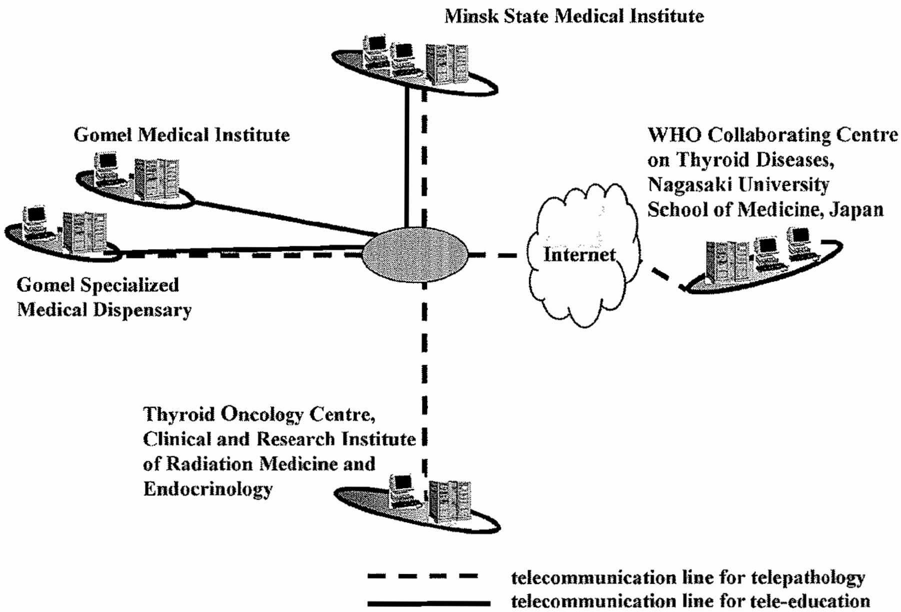

Fig. 1. Schematic illustration of main project goal related to the establishment of telecommunication links between participating institutions.

The establishment of the remote-area medical assistance system in Belarus should provide a double check in respect to diagnosis of thyroid diseases in children screened by ultrasound, quality control of medical data, appropriate guidance of cytological diagnosis, early and appropriate treatment and follow-up of patients. It should also promote information and experience exchange, and training and education of medical staff. The improvement of diagnostic quality will contribute to the better health risk assessment of ionizing radiation at international and national levels.

4. National participating institutions

The Ministry included in the project the following national institutions: Gomel Specialized Medical Dispensary (GSMD), Gomel Medical Institute (GMI), Clinical and Research Institute of Radiation Medicine and Endocrinology (CRIRME), Minsk state Medical Institute (MMI), and the Belarussian Centre for Medical Technologies, Information, Management and Health Care Economy (BelCMT). Each institution plays a role for the establishment of telepathology and tele-education (Fig. 1). At present, GSMD is in charge of thyroid screening of children living in radio-contaminated areas in Belarus. The establishment of a telepathology system will give the possibility for GSMD to obtain remote distance diagnostic consultations from MSMI and CRIRME. The latest institutions will obtain consultations from the Nagasaki University School of Medicine or some other WHO collaborating centre.

The establishment of a tele-education system will provide the opportunity for MSMI to play a key role in implementing training and education programmes, focusing on thyroid pathology, clinical diagnosis of thyroid diseases, and radiation health effect. The software for tele-education has been developed in a way that can be adapted to the web browser, such as Microsoft Internet Explorer.

5. Conclusion

The main goal of the project is to improve the early diagnosis and treatment of thyroid diseases in children affected by the Chernobyl accident through the development of a remote-area medical consultative system in Minsk and Gomel, and the WHO Collaborating Centre for Research on Thyroid Diseases, such as the Nagasaki University School of Medicine, Japan. This is just the beginning of introducing modern information and communication technology for Chernobyl problems. If one takes into account that about 4000 additional cases of thyroid cancer would be expected over the lifetime of those who were children and exposed to radiation at the time of the accident [5], then it becomes clear that further medical monitoring of this category of Chernobyl victims is vitally necessary. The use of health telematics technology for this purpose may facilitate the involvement of qualified experts at national and international levels in the strengthening of a local health care system and education of medical staff and students in territories affected by the Chernobyl accident.

Acknowledgements

We thank the kind assistance and cooperation by members of the Management Committee (Dr. K. Kiikuni from SMHF, Mrs. A. Kern from WHO and Dr. I. Zelenkevitch from the Ministry) and the Working Group (Drs. S. Yamashita and Tamashiro from SMHF and Mr. E. Glazkov from the Ministry). For further information on the activities of the project, the following website is available: http://www.who.int/peh/Radiation/healthtelepres.htm.

References

[1] G.N. Souchkevitch, A.F. Tsyb, Health Consequences of the Chernobyl accident, WHO Scientific Report, Geneva, 1996.

[2] S. Yamashita, Y. Shibata (Eds.), Chernobyl A Decade, Elsevier, Amsterdam, 1997.

[3] S. Yamashita, Y. Shibata, N. Takamura, K. Ashizawa, N. Sera, K. Eguchi, Satellite communication and medical assistance for thyroid disease diagnosis from Nagasaki to Chernobyl, Thyroid 9 (9) (1999) 969.

[4] N. Takamura, M. Nakashima, M. Ito, Y. Shibata, K. Ashizawa, S. Yamashita, A new century of international telemedicine for radiation-exposed victims in the world, J. Clin. Endocrinol. Metab. (in press).

[5] E.D. Williams, D. Becker, E.P. Demichik, P. Nagataki, A. Pinchera, N.D. Tronko, Effects on the thyroid in population exposed to radiation as a result of the Chernobyl accident, Proceeding of an International Conference, Vienna, 8–12 April 1996, International Atomic Energy Agency, Vienna, 1996, pp. 207–230.

Summary and future scope

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Comments and discussion

Moderators:
Dillwyn E. Williams, *Joint Director, Thyroid Carcinogenesis Research Group, University of Cambridge, UK*
Kenzo Kiikuni, *Chairman, Sasakawa Memorial Health Foundation, Japan*

Invited Speakers:
Nikolay A. Krysenko, *Chief, Gomel Region Health Care Department, Belarus*
Vladimir V. Martynovskiy, *Chief, Mogilev Region Health Care Department, Belarus*
Aleksandr M. Yakovlev, *Chief, Bryansk Region Health Care Department, Russian Federation*
Vladimir V. Elagin, *Chief, Kiev Region Health Care Department, Ukraine*
Zhinoviy M. Paramonov, *Chief, Zhitomir Region Health Care Department, Ukraine*
Bruce W. Wachholz, *Chief, DNA and Chromosome Aberrations Branch, National Cancer Institute, USA*
Shigenobu Nagataki, *Chairman, Radiation Effects Research Foundation, Japan*
Diederik Teunen, *Scientific Officer Directorate General Research, Nuclear Fission and Radiation Protection J4, European Commission*
Michael N. Repacholi, *Coordinator, Occupational and Environmental Health, WHO, Switzerland*

Kenzo Kiikuni
I hope you enjoyed the last coffee break. Now we are going to have the final part of our 2-day symposium, i.e., we are going to have a special session: “Lessons from Chernobyl and message for the 21st century.” We are, of course, in the 21st century already. I think the 20th century made many historical events including the Chernobyl disaster. Thus, I would like to invite the distinguished people from the five centers as well as international experts to comment on the lessons we have had and the message for the 21st century. The first speaker is Dr. Krysenko from Gomel Region Health Care Department. Dr. Krysenko, please take the floor.

Nikolay A. Krysenko
Distinguished Chairman, dear ladies, gentlemen and colleagues:
Fifteen years have elapsed since the day of the Chernobyl catastrophe. All the medical consequences, which have mostly been estimated today and led to further work, are rather complicated and considerable. The information announced during this symposium, due to

0531-5131/02 © 2002 Published by Elsevier Science B.V.
PII: S0531-5131(01)00849-4

the purposeful and scientific work by Japanese experts and Sasakawa Memorial Health Foundation, allowed us to estimate more thoroughly, purposefully and systematically the medical situation existing in Gomel region after the Chernobyl catastrophe. As everyone must have heard and understood, valid scientifically proved consequences to the health of the population in Gomel region are quite complicated. They are the reflection of that complicated radiation situation that existed since the very first hours of the accident at the fourth reactor of the Chernobyl Nuclear Power Plant. Today, we must take into consideration that the population of Gomel region, being unprotected during the first days after the accident, was later found with those complicated and non-forecasted consequences, which were reported during the 2 days of the symposium. Perhaps, among the most difficult fields for research are thyroid disorders and consequences of that complicated iodine strike which the unprotected population of Gomel region had been exposed to. Therefore, I would like to express special gratitude to the scientists of Japan, to Prof. Shigematsu, Prof. Nagataki, Prof. Yamashita, Prof. Shibata and others, who in the frames of joint projects during these past 10 years not only helped us estimate the situation but also helped with the correct diagnosis, correct treatment, and in the beginning of prophylaxis of those considerable complications that began to happen in the Gomel region population.

I would like to draw your attention to the fact that 15 years is a very short period for risk estimation and forecast for appearance of various diseases, and these are not only thyroid disorders. Today, we are faced with different, more complicated problems. Because, for example, if there are 200 cases of thyroid cancer registered in Gomel region per year (40 cases of this number are children and adolescents), then the increase of other kinds of malignant tumors is quite significant. As for the disease rate, there are 360 cancers in 10 000 of the population; the Gomel region is leading in the Belarus Republic, having risen from 240 in 10 000 to 360, and this problem is a very acute problem for further diagnosis, treatment and prophylaxis. Therefore, I, with a great hope, express today a confidence that our scientifically based joint studies will continue in the future because there are a lot of problems to be solved today not only concerning tumors and leukemias but also ordinary somatic disorders, which may be caused by various factors, which affected us humans after the Chernobyl catastrophe. Thank you for your attention.

Kenzo Kiikuni

Next speaker is from Mogilev Region Health Care Department. Dr. Martynovskiy will present his comments.

Vladimir V. Martynovskiy

Dear Chairman, dear ladies and gentlemen, dear colleagues:

First of all, I would like to express our true gratitude to Mr. Sasakawa and to all those who were involved in the work of Sasakawa Memorial Health Foundation and helped our Mogilev region to solve its problems. I am especially happy to stress it out because I happened to start this work 10 years ago when I worked as Chief Physician of Mogilev Regional Diagnostic Center.

Our Mogilev region is one of the regions that have been suffering the consequences of the accident at the Chernobyl station. More than 200 000 people, of whom more than 40 000 were children, more or less have been suffering the consequences of the Chernobyl accident. There are about 6000 people living in Mogilev region who were the liquidators of consequences of the accident at the Chernobyl station. They are not "witnesses", as reported by one of my colleagues, but real participants of the liquidation of consequences of the accident at the Chernobyl Nuclear Power Plant. The Chernobyl accident required from us, doctors of Mogilev region, additional responsibility, efforts and funds for minimizing the medical aftermath of the accident. We have built our work during the past 15 years aiming to improve medical equipment at the base of the Mogilev region and many medical institutions, which were opened during the last 15 years due to the efforts of our government and local governments aiming to work with consequences of the accident at the Chernobyl station.

Fifteen years have elapsed and we are now in the new century, but unfortunately, the problem of Chernobyl remains. I think that many problems and matters have appeared and that they should be solved today by the medical staff of our country and region, and by the world community. It is good that the results of scientific research presented in the 2-day symposium were in a rather narrow field. We more or less understood the details of thyroid disease problems, which we have met for years, and today we may say, though there is no complete confidence, that this pathology is connected to some degree with the accident which occurred in our country.

Dear colleagues, in my opinion, the Chernobyl problem is not so narrow as thyroid pathology goes. The Chernobyl problem is a wider aspect of medical care for minimizing the consequences of the accident at the Chernobyl station. These are the liquidators, about whom I have already spoken today, the people who took part in the liquidation of the consequences of the accident. Unfortunately, many of them have gone away already; this is a so-called psychic status of the people living in the territories contaminated by the accident at the Chernobyl station. It is a huge problem which we feel still exists today. We now have a high level of incidence of various diseases as well as thyroid disorders. In my opinion, there is a need to carry out deep epidemiological research of cardiovascular diseases and others, about which we may say to you distinctly and full of confidence that they are connected to some degree with a complex of terms that influence the health condition of our population.

Distinguished Chairman, I would like once more, on behalf of our regional government, medical staff and the people of the Mogilev region, to express appreciation for the work that was done in these past 10 years. This work is invaluable and will allow us to treat in some way a determined piece of work, and to say with some degree of confidence that we can do something for our people. Thank you for your attention.

Kenzo Kiikuni

Thank you, Dr. Martynovskiy. The third speaker is from Bryansk. Dr. Yakovlev, please.

Sergey N. Fetisov

Deputy Chief of Bryansk Region Health Care Department, on behalf of Dr. Yakovlev.

Distinguished Chairman, dear ladies and gentlemen, colleagues:

Today, we are drawing a bottom line for the minimization of medical and social aftereffects of the accident at the Chernobyl Nuclear Power Plant. Actually, there is a lot of work to be done during these years. The accident happened in a united country named The

Soviet Union, and today, its consequences should be overcome by three independent states. Problems met by frontier areas are almost the same, and during the present conference, we managed to hear, feel and understand the fact. Not a few were done during the last years and not so few funds have been invested to the consequences, but the socio-economical situation in contaminated areas, including the Bryansk region, remains difficult. The incidence rate of many kinds of diseases in Bryansk region is higher than the average rate in Russia and it was reported yesterday. The mortality rate has increased while the birth rate has decreased in seven southwest areas of the region. These areas are most contaminated by the accident, and the natural decrease in the population is 15% higher than the average decrease in the region. The disease rate in main categories is higher than the average in the region by up to 60% in adults and 3–3.5 times in children. During the last 5 years, as reported by our center and presented in a report of Prof. Ivanov as well, the prevalence of malignant tumors exceeded the average ones in Russia by 10–15%. Stable prevalence all over Russia can be seen in the incidence rate of tumors of stomach, lungs, hemopoietic and lymph tissues. Index of disease rate of thyroid cancer in children exceeds those of all Russia during the last 10 years by more than two times. All of these were shown at the conference.

I would like to say, as an oriental wisdom says, that if you want to feed a person once, give him a fish, but if you want the person be replete constantly, give him a fishing rod and teach him how to fish. Ten years ago, Sasakawa Memorial Health Foundation did just the same way. During 5 years from 1991 to 1996, there was the medical equipment donated by the foundation and several measures were taken that allowed us in the next 5 years to work for the health of the Bryansk region population. I must say that the work done by the distinguished foundation is not a waste and will not be wasted in the future. As used to be said not so long ago, the deed of Sasakawa lives and wins. Finally, I would like, after the approval of Mr. Chairman, to invite the Chief Physician of Bryansk Regional Diagnostic Center to the stage.

Dear representatives of Sasakawa Memorial Health Foundation, let us, on behalf of the Bryansk region administration and the people for whom you have worked for these past 10 years in Bryansk region, thank you for the work you did and hand you a small and very modest present for the foundation.

Sergey Ye. Krivenko
Chief Physician, Bryansk Regional Diagnostic Center No. 2

This picture entitled "A path in the forest" was made by our local artist. We hope that this path will connect the foundation and us for a long time and we will be happy to see you in our land any time. On behalf of the citizens of the town whom you have helped, let me hand diplomas to Mr. Sasakawa, to my favorite Santa Claus Prof. Kiikuni, to Prof. Yamashita who knows our center so well not only as a doctor but also as an administrator by advising me at his visit what to do next, to Prof. Fujimura and to Prof. Shibata, and I, with great pleasure, hand the diploma to Mrs. Maki whom I respect very much. Thank you.

Kenzo Kiikuni
This is certainly an unexpected surprise but I really appreciate the work of all the five centers. The next presentation is by Dr. Elagin from Kiev. He is the Chief of Kiev Health Care Department and is one of my good friends. Where is he?

Aleksandr Alekseenko
Deputy Chief of Kiev Region Health Care Department, on behalf of Dr. Elagin.

Dear Chairman, dear ladies and gentlemen, dear colleagues:

Dr. Elagin could not attend the meeting for some reasons and I will make a presentation instead of him. My name is Alekseenko Aleksandr Aleksandrovich. Let me first of all express my gratitude to Mr. Sasakawa, to all who organized this symposium and to those who work in Sasakawa Memorial Health Foundation for the opportunity to meet with the specialists from the countries that take part in the symposium. They are the specialists from Belarus, Russia, Ukraine and Japan who investigate all the medical problems in all territories contaminated by the Chernobyl catastrophe. One of the territories most contaminated by the Chernobyl accident is Kiev region where the Chernobyl Nuclear Power Plant is situated and about a million (excluding the Kiev city population) of affected people are living. One-fourth of them are children, that is, 25 000 are the affected children. Under the law of Ukraine about the status of affected people, there are two matters for the practical medical staff to take into consideration—screening of the affected population and national registry. Every year, the medical staff of the region carries out a total screening of the affected population. It is a considerable amount of work, as you understand, to have more than a half of the region's affected population (1 800 000 in total) and to carry out their screening every year. However, we carried it out in spite of anything, mobilizing the resources and power to do that. If you see the results of our work and screening, it is obvious that the health condition of the affected population becomes worse year by year. We are worried about the general health state of the population affected by the Chernobyl accident, primarily that of those living in the radio-contaminated territories. There are 25 districts in the region in total and more than half are radio-contaminated, but the affected people live in all the districts. The influence of a complex of factors typical for such a catastrophe caused an evident increase in the disease rate among the affected people, primarily among the population of children. Particularly, an increase may be observed in tumors, diseases of blood and hemopoietic organs and congenital abnormalities. If we look at the structure of the screened adult population, we will see that there were 33.5% of adults practically with no abnormalities and only 13% in 2000. In the last and previous years, there were only 15.5%. The structure of the screened children population looks as follows: in 1989, 60.2% of the children population was considered as normal while in 2000, 17%. In 2000, according to the results of the screening of those who took part in the liquidation of consequences—and there are a lot of them in our region—almost one-fourth of the affected people were liquidators, and of the screening of those who took part in the liquidations of consequences, only 9.7% were considered normal, while in 1999, 12% were normal. As is seen from the previous data, the normal population in adults and children decreased by more than three times during the last 10 years. The total number of abnormalities in the adult people affected by the Chernobyl accident is 16 500 people, which is 7.5% higher than that in 1998. The prevalence of disorders in the affected and non-affected population of the region looks as follows: the prevalence in the total population is 142 000, in the affected population, 153 000, and in the non-affected population, 128 000. Thus, the difference seems to be quite large.

The screening has been carried out for 14 years already and its results show that the health condition of the affected population is going worse. The prevalence of general disorders in the children population was 16.7 per 10000 in 1994, in 1997, 18.6, and in 1999, 24.0 — a similar picture as the one in the adult population. We see a very obvious tendency of an increase in tumors in the children population. We can present the data before 1989, and before the accident, there was not any case of thyroid cancer in children registered in the region, was there? Maybe there was a single case. In 1990, we began to register thyroid cancer in children. At present, there are 62 cases of thyroid cancer in children registered in the region. During the period after the accident, a considerable decrease in the health condition of the participants of liquidation is visible. The number of healthy people, who were young and healthy at the time of the liquidation of consequences, considerably decreased during this period. An increase in the disease rate in liquidators was observed due to diseases of the nervous system, sensory organs, endocrine system and blood circulation system. It may take a long time to make an analysis of the disease rate in the adult and children population and liquidators. Even according to the figures I have already mentioned, it is obvious and cannot be ignored that the health condition of the people affected by the accident is going worse and we must take some measures. We register the results of the screening into the national registry. There is a flexible system of registering people affected by the accident at the Chernobyl Nuclear Power Plant created under the leadership of the Ministry of Health of Ukraine. It is not necessary to speak much about that. All were discussed in this meeting before, all are presented now and all will be discussed after me — all these are consequences of a lesson which we learned from the Chernobyl accident in 1986. As Mr. Chairman said today, we are already living in the 21st century and there is no need for a message to it. I just want to wish all in this hall, all affected and all living in these territories, that the Chernobyl catastrophe would never be repeated. Thank you.

Kenzo Kiikuni

Thank you very much Dr. Alekseenko for your presentation. Our last speaker from the five regions is Dr. Paramonov from Zhitomir. You have the floor.

Vladimir K. Golovakov

Deputy Chief of Zhitomir Region Health Care Department, on behalf of Dr. Paramonov.

Distinguished Chairman, dear ladies and gentlemen, dear participants of the International Chernobyl Sasakawa Symposium:

Unfortunately, Mr. Paramonov could not come. I am his deputy and will represent the Zhitomir region. Let me, on behalf of the state administration of Zhitomir region, Zhitomir Health Care Department and the people of Zhitomir region, express true gratitude to the distinguished Mr. Sasakawa, staff of Sasakawa Memorial Health Foundation, Japanese scientists, Prof. Kiikuni, Prof. Yamashita and Prof. Fujimura, and to many other participants of the Chernobyl Sasakawa Health and Medical Cooperation Project for the help they rendered to health organizations and to the population of Zhitomir region. Zhitomir region is one of the territories in Ukraine most affected by the accident at the Chernobyl nuclear station. In 1986, among the 92 settlements of unconditional evacuation, 63 were located in Zhitomir region. Also, among 835 settlements of guaranteed voluntary evacuation and 1290 settlements of thorough dosimetry control, 301 and 363 settlements were located in the region, respectively. In 2000, 40% of the total population of Zhitomir region lived in contaminated territories. I would like to draw your attention to the fact that in comparison with 1986, the region's population decreased by 8.9%. Furthermore, the population of the northern districts of the region decreased by 9.4% in the period of 1989–1995, and by 14%, up to 1 January 2001. This was greatly influenced by migration and negative index of reproduction, which have been observed since the end of 1988. These factors not only led to the present situation of demographic crisis but also will lead to impossible improvement of the situation in the next 10 years of unlimited installation of social and economic measures from the state and government, and support by humanitarian funds and public organizations. Since the beginning of the post-accident period and up to the present moment, we have received a significant financial assistance from Sasakawa Memorial Health Foundation. With the help of a mobile clinic laboratory donated by the foundation, we performed medical examination of children living in the most distant villages affected by the accident at the Chernobyl station. The equipment donated to Korosten Inter-Area Medical Diagnostic Center gave an opportunity to hold diagnosis at a high level. There are two ultrasound equipments, Aloka 520 and 630, two dosimeters for the measurement of Cs-137 specific activity in the body, a stationary and a mobile one, automatic blood analyzer Sysmex K-1000 and NE-7000, immuno-ferment blood analyzer for hormones, deep freezers storing blood samples of examined children, thermostat, lectioscope and many others. We were also donated a 30-seat bus, Toyota Coaster, to transport children to the Korosten Inter-Area Medical Diagnostic Center for examination. When the second building of the Korosten Inter-Area Medical Diagnostic Center was opened, the foundation gave assistance in a sum of 30 300 UAH for the purchase of furniture. In the period of 1991–1996, about 36 000 children from the northern districts of the region, who were affected by the accident at the Chernobyl Nuclear Power Plant, were examined. Ten cases of thyroid cancer were found in children, who were operated and are now under follow-up in the place of residence. Autoimmune thyroiditis was found in 210 (0.6%) and other abnormalities were found in 11 219 (31.2%). Anemia was found in 8.4% of the children, leukocytosis was found in one child and Werlhof's disease was found in four children. After the completion of the project for screening children, the work has been continued owing to the assistance of Sasakawa Memorial Health Foundation. Medical help to the affected population remained at the same level owing to the assistance of Basic Human Needs (BHN) Association in Tokyo which has provided the Korosten Inter-Area Medical Diagnostic Center reagents and consumables annually during the last few years. Great thanks for that to Mr. Nobusawa, the President of BHN and Mr. Shinohara, the General Secretary of BHN. After the project was over, the connection between the Korosten Inter-Area Medical Diagnostic Center and Sasakawa Memorial Health Foundation has not been cut. The foundation gave assistance in transport repair and in 2001 donated an ultrasound equipment Logic 100α. During these years, Japanese specialists and scientists visited the center and rendered practical help. Ten specialists of the Korosten Inter-Area Medical Diagnostic Center were trained in Japan by medical organizations of Hiroshima and Nagasaki. Visits to the region, contact with the people and lectures to the people of the region, which were made by Japanese specialists

since 1991, mollified psycho-emotional tension in people of the region, particularly in citizens of Korosten city. We are grateful to Japanese specialists and to Sasakawa Memorial Health Foundation for a great help to health care in Zhitomir region. By the joint efforts, we managed to provide the region's population with the first class medical care. I wish the cooperation be continued, and friendship and mutual understanding be strengthened. Thank you for your attention.

Kenzo Kiikuni

Thank you very much for your comment. I will now hand over the task of chairing the next session to Prof. Williams.

Dillwyn E. Williams

Thank you, Prof. Kiikuni. Now, I have received the task of chairing the second part of the session in which more international aspects will be presented. Dr. Bruce Wachholz, please, from National Cancer Institute of the United States to make your contribution to "Lessons from Chernobyl and message for the 21st century."

Bruce W. Wachholz

Chairman Kiikuni, Chairman Sir Dillwyn, esteemed scientists, distinguished guests, ladies and gentlemen:

The past 2 days of this meeting have focused on the tragedy of Chernobyl, and on the generosity and contributions of the medical and humanitarian resources that Sasakawa Memorial Health Foundation (SMHF) has provided over the past 10 years to help define the resulting health effects among the exposed populations in Belarus, the Russian Federation and Ukraine. It is timely that the foundation sponsors such a meeting upon the completion of the Chernobyl Sasakawa Health and Medical Cooperation Project, especially since it is coincident with the 15th year after the accident. It also is thoughtful of the foundation to invite other organizations that have been active in the Chernobyl area to reflect upon some of what they have observed and learned during the intervening years. The National Cancer Institute (NCI) is most grateful and appreciative for this opportunity, but with just a few minutes of time, I can only touch upon reflections that are, therefore, limited to general remarks. These can be grouped into a few major categories, each of which I will comment upon briefly: international and national issues, scientific observations, and if permissible, a few remarks of a more personal nature.

When looked at from a perspective of international concern and involvement, previous civilian nuclear accidents such as Three Mile Island and Windscale did not mobilize the international community with respect to health consequences to the extent that the Chernobyl accident did, perhaps in part, because these events affected primarily local populations in the country where the facility was located; moreover, as momentous as these events were, the resulting health consequences were not comparable with those associated with the Chernobyl accident. Even fallout from atmospheric nuclear weapons tests affected mainly the downwind populations which, for the most part, were within national jurisdictions. With Chernobyl, however, we learned suddenly and with varying degrees of concern that the impact and consequences of a major civilian nuclear accident are not necessarily confined to the borders of the country in which it occurs, but also affect both adjacent and more distant countries with respect to public health and medical care, psychological stress, social disruption, agricultural difficulties, economic consequences and also in other ways. Chernobyl dramatized the need for improved interaction and collaboration among the international agencies and between them and national authorities and the public. This has motivated both the multiple agencies of the United Nations, along with other international organizations (e.g., the Nuclear Energy Agency), and international and national radiation protection authorities to reassess their guidelines and operational plans for major emergencies and to revise and coordinate their several responsibilities. (An example of this is an international nuclear emergency exercise that was to be carried out last week under the joint sponsorship and coordination of five international organizations.) These changes hopefully will be beneficial if and when there again is a need for coordination and cooperation between and among the international agencies and the affected country in response to another major nuclear accident.

Individual countries also might benefit from improvements in cooperation among their various national agencies and institutes. Although this observation no doubt is applicable to a number of countries, I can refer only to my own. Following the Chernobyl accident, there were within the United States a number of government agencies and non-government organizations that offered technical or humanitarian assistance and/or that expressed interest in the potential for environmental and biomedical research possibilities. This assistance and/or interest was increasingly apparent once it became possible to communicate with and visit our colleagues in Belarus, the Russian Federation and Ukraine. For example, following an agreement between USSR and the US in 1988 to cooperate in the area of research on the safety of civilian nuclear reactors, eventually at least eight US government agencies were involved in some Chernobyl-related health and environmental activity pertaining mainly to cooperative research possibilities although some of these agencies also were involved in programs of cooperative technical assistance. (In addition, numerous non-government organizations were involved in Chernobyl-related activities, many of which focused on humanitarian efforts.) Obviously, it took time to clarify the roles, responsibilities and areas for cooperation among these agencies, and I suspect that perhaps similar situations existed also in at least a few other countries. This was a learning experience for all of us.

There has, of course, been an immense body of data and information pertaining to the accident that has resulted from a large variety of studies carried out over the past 15 years by scientists within each country, often in cooperation with foreign investigators, and the proceedings of this meeting will add to that database by including contributed papers from many of these scientists. Anyone reviewing the relevant literature cannot help but be impressed with all that have been learned of the consequences of the Chernobyl accident and by the numerous governments and organizations that have financed and otherwise supported this work. However, there still is much to learn, and I am appreciative that my government continues to support Chernobyl-related studies.

Although time does not permit a review of the many specific scientific lessons that have been learned, I would like to mention a few general lessons that may be relevant.

First, we have learned to be more open to findings that do not conform to general expectations, i.e., the prevailing paradigm. As you know, there was considerable skepticism when the increases in thyroid cancer were first reported in Belarus and Ukraine with respect to both the number of reported cases and their latent period; these reports did not conform to the then-prevailing paradigm. While causes of thyroid cancer other than radiation (e.g., I-131) were initially hypothesized (e.g., more intense screening, ascertainment bias, diagnostic uncertainties), these suggestions were to some extent driven by the reluctance of scientists to attribute the findings to radiation exposure, and therefore, there was a perceived need to attribute the findings to a cause other than radiation. Obviously, the findings were real and we now know that the former paradigm with respect to thyroid cancer and exposure to I-131 was incorrect, that it has changed because of Chernobyl and that a new paradigm is now accepted although we still are attempting to discern the relationship between exposure to radioactive iodine and thyroid cancer. As recently as yesterday, another paradigm is being questioned. We heard of a reported increase in thyroid cancer among persons born after the accident and after the time when exposure to I-131 would have been possible. The basis of this report also needs to be investigated and perhaps, again, another paradigm will need to be reconsidered.

Second, we have learned to cooperate with each other collectively. An excellent example of this cooperation is the international financial and management support from five countries (the United States, Japan, Belarus, the Russian Federation and Ukraine) and two international organizations (the European Commission [EC] and the World Health Organization [WHO]) to fund and manage the Chernobyl Thyroid Tissue, Nucleic Acid and Data Repositories in Belarus, the Russian Federation and Ukraine, which you heard about earlier today. Even this success required several years of negotiation, good will and understanding among the seven participants in order to satisfy the diverse laws, policies and requirements of each of them, and the NCI is pleased and proud to be a partner in this achievement.

Third, we also have learned to cooperate with each other in binational relationships. Given our respective histories, interests and agendas, to say nothing of strong personalities and numerous practical, political, regulatory and/or legal issues, it is a tribute to everyone involved that over time, we learned what each party could contribute and how together we could accomplish scientific and medical research that might not have been successful without personal, institutional and government cooperation and collaboration. Examples of these include the successful efforts by the three countries to work initially with the International Atomic Energy Agency and the WHO, and subsequently with SMHF, the NCI, the EC and the other governments and organizations. For example, one lesson that evolved from this experience is the need for each party to clearly understand the expectations and constraints of the others in order to minimize potential discord, e.g., defining the overlap or the boundaries between humanitarian assistance and research objectives.

Should the need for such international and/or binational cooperation arise in the future, we hopefully will have learned through this experience, will be more candid with each other and will come together in a much more timely manner than was the case with Chernobyl.

Finally, on the personal level, there are many things that I have learned: about people, countries, cultures and the resolution of bi- and multi-national scientific, financial, administrative and governmental challenges, both in other countries and in my own. The privilege of representing the NCI and the US in laying the groundwork and developing the infrastructure for cooperation between NCI and the scientists and governments of Belarus and Ukraine to carry out long-term epidemiology studies in those countries of the relationship between exposure to radioactive iodine and the subsequent development of thyroid cancers has again demonstrated that mutually sincere efforts can overcome decades of alienation and distrust— and for me at least, result in experiences and friendships that at one time were unimaginable.

In conclusion, what have we learned from the Chernobyl accident? That we are all affected by the actions of each other; that, since the radioactivity released into the environment respects no national boundaries, international as well as national cooperation is mandatory following a major nuclear accident; that our minds must be opened to unexpected observations; and that professional and personal commitment and goodwill can overcome the potential challenges of governments, cultures and language, and in the process, lead to professional accomplishments and satisfaction and to personal rewards and friendships.

Again, I wish to congratulate Sasakawa Memorial Health Foundation for their prompt response to the request of the former Soviet Union for assistance and for implementing a remarkable and successful program over the past 10 years.

Thank you for your attention.

Dillwyn E. Williams

Next, please, Prof. Shigenobu Nagataki of Radiation Effects Research Foundation in Japan.

Shigenobu Nagataki

Thank you. This is a session of "Lessons from Chernobyl and message for the 21st century," so I will try to deliver a message from Japan because Japan is the only country that received atomic bombing by which more than 70 000 people died and hundreds of thousands people suffered from the effects of radiation. This information shows what really happened in the 20th century from the standpoint of radiation exposure, which includes the atomic bombing to Hiroshima and Nagasaki, nuclear tests in Nevada, Semipalatinsk and Marshall islands, nuclear accidents in South Ural, Chernobyl and Three Mile Island, and also medical use in therapy and diagnosis. Financial problems should be solved by compensation for radiation-exposed victims from the standpoint of policy and publicity. Here, we have close information from the atomic bomb survivors, which gives us the universal standards for radiation protection.

First, I would like to talk about the future direction through the atomic bomb survivors' studies and then about the international collaboration through our lessons from Chernobyl. Finally, I would like to talk about the importance of bridging science and policy, taking radiation exposure problem as an example. An overview of the studies on A-bomb survivors indicates the necessity to continue traditional epidemiological studies that have been so important during our own 45-year experience in RERF, focusing on the health effects of radiation by the atomic bomb. It should be continued and new molecular biology studies should be introduced to clarify the basic mechanism of radiation-induced carcinogenesis and a radiation dose effect. It may be possible through the establishment of an invaluable storage of some biological samples at local centers for the survivors. Now, we change our discussion from the present situation to a future plan of Chernobyl. As for the internal collaboration, we have to recognize the difference between scientific and humanitarian collaboration. Both are important but we have to bear in mind what the scientific collaboration and humanitarian collaboration are, respectively. The scientific one is to find out whether they are "Hibakusha" or not. Alternatively, it has to be investigated if there is an influence of radiation on humans. The humanitarian approach is to support the general population living in the radio-contaminated regions, to support the general population without knowing whether they are "Hibakusha" or not and to support them much more even they do not know whether they are "Hibakusha" or not. This is a big difference but both are important. We have to recognize, as another example, what is now ongoing regarding a support from Japan to Kazakhstan. Next issue of importance is the international collaboration which is most important in exchanging information and in avoiding duplication that we experience very often during the course of the study of Chernobyl. We can publish all results of studies, from scientific studies or epidemiological studies to medical studies. At the same time, as they pressed questions to us yesterday, there is a concern about the use of radiation: nuclear power, medical treatment, waste management, etc., so what we can do now is to publish and explain what we have obtained from our experiences. We also have to bear in our mind that international- and nation-specific decisions can be made according to public understandings and opinions. The policy-making process should take scientific and humanitarian aspects into consideration. I think it is important in the 21st century to breed science and policy in the field of radiation. It is important for social solutions. Scientific experts, regulators, policy makers and radiation specialists may have to collaborate to reach consensus around people who have taken different technical regulatory even social rank and political positions on important social solutions. It is important to make a consensus and develop a strategy for formulating national and international policy based on available scientific information on important social solutions. Important social solutions may include the interdiction of nuclear weapons, utilization of nuclear energy, nuclear waste, low dose radiation, radiation protection, emergency and volunteer risks, compensation to victims and expositions to the public. Thank you very much.

Dillwyn E. Williams

Next, please, Dr. Diederik Teunen from the European Commission.

Diederik Teunen

Ladies and gentlemen:

It is my pleasure to participate as representative of the European Commission in this important symposium and to present to you today our views on the past experiences and the way forward.

In the early days after the Chernobyl accident, some measures of cooperation between the European Union and the former Soviet authorities were established, including the provision of large numbers of small dosimeters to help assess the extent of the radioactive contamination. Also, the Radiation Protection Research Program 1985–1989 of the European Commission was revised to include 10 coordinated multinational projects for assessing and mitigating the short-term consequences of the accident.

In 1991, soon after the start of the third research framework program, the European Parliament granted the European Commission a specific research budget for the study of the consequences of the Chernobyl accident of about 20 million.

Six years after the devastating accident in 1992, the European Commission has entered into a historic agreement called 'Agreement for International Collaboration on the Consequences of the Chernobyl Accident' with the three republics most directly concerned: Russia, Belarus and Ukraine. This agreement formalised the research cooperation and allowed for close collaborative field-research work to be carried out on the territory of the three states. Since that time, an extensive program was initiated involving scientists from 40 teams from the east and the west to study the nature of the radioactive contamination resulting from the accident, to broaden the technical skills needed to control this type of accident in the future and to improve emergency management procedures. Appropriate scenarios for environmental decontamination were designed and the assessment of long-term health effects was started, resulting in the finding of excess numbers of thyroid cancer in people, being children and adolescents at the time of exposure.

A coordination board was established with participation of all partners to supervise the implementation of the research projects. Today, this board is still an important instrument for the coordination of the international efforts and meets on a regular basis to discuss results and future needs.

This scientific collaboration not only has allowed us to gain a great deal of experience both as regards the emergency preparedness and health effects of ionizing radiation but also helped to alleviate the suffering of the affected populations. Therefore, it is the European Commission's conviction that close collaboration of this type in a conditio sine qua non for guaranteeing good scientific progress in the future. One excellent example of the success of such approach is the 'International Cooperation to Establish Post-Chernobyl NIS Thyroid Tissue, Nucleic Acid and Data Banks' (NISCTB), a collaborative action with Sasakawa Memorial Health Foundation, WHO, NCI and institutes from the three republics. The cooperation has a well-defined operational structure and an internationally agreed protocol, allowing the worldwide scientific community access to important study material. Therefore, the data bank project will continue to be funded by the Fifth Framework Program for the next 48 months.

In addition to the research cooperation, I should also mention that the EC has been strongly involved in the technical assistance through its TACIS program, which has contributed to the safety of the sarcophagus, the decommissioning of other reactors and the decontamination of the site and its surroundings.

The European Commission looks forward to a future collaboration with all the interested parties present here today.

Thank you for your attention.

Dillwyn E. Williams

Finally, please, Dr. Mike Repacholi from the World Health Organization.

Michael N. Repacholi

The World Health Organization was involved from the very beginning in the assistance programs for people affected by radioactive materials given off during the Chernobyl accident. While large reactor accidents of this magnitude are rare, there is a real possibility of such an accident occurring again in the future.

It is extremely important that the maximum amount of information be gained from such a disaster to ensure that the consequences can be minimized as much as possible. While there was a coordinated effort to reduce the impact of the accident, there are many lessons that need to be learned to be better prepared in the future. Some of these are itemised below.

- Improve coordination of programs by international, government and non-governmental organizations to provide medical and humanitarian assistance to potentially large numbers of exposed people.
- Responses should address the fact that accidents cause psychological stress, social and economical consequences and that these need to be dealt with effectively and as soon as possible.
- Establish effective training on protective measures for emergency and clean-up workers, firemen and medical staff to reduce their radiation exposures.
- Infrastructure for public health actions and support should be in place well before accidents.
- Have iodine prophylaxis available for people in case of possible exposure to radioiodine, but information on simpler measures such as not drinking milk or other specified food products should be made available.
- As soon as possible, after the accidents, establish registries of people overexposed to radiation and organize their long-term monitoring.
- Establish a radiation measurement and dosimetry system to allow personnel doses to be determined (for medical treatment and future studies).

While these are but a few of the lessons that can be learned from the Chernobyl accident, there are many more. There is NO excuse for not being fully prepared for another major nuclear accident of the size of Chernobyl. We have had 15 years to be prepared.

Dillwyn E. Williams

Thank you very much to all the speakers for the contributions. We have time for a few brief contributions from the floor or questions that anybody wishes to rise about a particular point... It just seems to me that we have learned a great deal about a role of radioactive iodine that causes thyroid cancer and the importance of age at exposure as a factor of sensitivity. However, as several speakers told us, we still have not done enough in terms of international cooperation to help studies of consequences other than thyroid diseases, in particular, as Mike Repacholi told us, probable effects of living in environments of low level radiation. We also have to consider how the international community responded to Chernobyl and how we can ensure that we will respond, perhaps, in a more coordinated fashion if there is another accident. It seems to me that by globalization, we have a large-scale economy which will be accompanied by large-scale disasters. We may have not only nuclear problems but also other disasters which will affect several countries. We still need to know how to organize cooperation and how to overcome some of the problems of sovereignty. Perhaps, you have now time to think of the question... Oh, if not... Do you have anything to say to us, Prof. Kiikuni?

Kenzo Kiikuni

If not, we will move to the closing ceremony. Prof. Tsyb, Vice Chairman of the Organizing Committee, would present the Moscow Declaration, or more precisely, the Sasakawa Declaration in Moscow. I invite Prof. Tsyb. Copies of the draft of the resolution are distributed, one in English and the other in Russian.

Anatoly F. Tsyb

Dear colleagues, friends, participants of the symposium:

I would like to say a few words as closing remarks. During the past 2 days, we have witnessed the procession of Sasakawa Memorial Health Foundation, the peaceful and humanitarian procession in our land, especially in ecologically polluted territories. That was a parade of the diagnostic centers of the foundation and was a conclusion of the work of 15 years. We have seen that there are significant achievements in practical medical help as well as in scientific work. I would like to say that I would sign under every word that Dr. Wachholz said in his beautiful presentation here. I liked very much his presentation in the style and content and the postulates he presented including the disproval of paradigms that we had in minds before the Chernobyl accident. Now, let me present to you the Moscow Declaration, or more precisely, the Sasakawa Declaration in Moscow as Prof. Kiikuni said.

The Moscow Declaration or Sasakawa Declaration in Moscow (see page 159) was read out by Prof. Tsyb.

Kenzo Kiikuni

Thank you very much Prof. Tsyb for reading clearly the Sasakawa Declaration in Moscow. I hope everyone is in agreement with this Sasakawa Declaration in Moscow. If there are any questions or comments, please raise your hand. Would you agree with this Sasakawa Declaration in Moscow, 31 May 2001?... Thank you very much.

Anatoly F. Tsyb

Thank you very much, friends. See you next time. Thank you.

Dillwyn E. Williams

I wish very briefly, as everybody did, to express thanks to the organizers of this symposium, particularly to my co-chairman Prof. Kiikuni, to Dr. Shigematsu as chairman of the organizing committee, to Mrs. Maki and to the staff behind the scenes. Particularly, all of us have benefited by the generosity of Sasakawa Memorial Health Foundation and by the wisdom of Dr. Shigematsu as the chairman of the Sasaakawa Chernobyl Scientific Committee. I think he will still give us that wisdom as he seems to be completely unchanged through the years. Dr. Shigematsu and other people of this committee, I think, performed outstanding studies at the five centers, supported this conference, supported the five centers and will continue to support the tissue bank. Furthermore, the foundation gave all of us an example of the way to organize the efficient study, produce supreme results and support international collaboration and development of friendship between nations.

We have a saying in English that you should not carry coals to Newcastle. That means that you should not give anyone what he or she already has. However, I would like to ask

Mr. Sasakawa be kind enough to accept a very small gift which has just been published in Britain. This is an English book about Japan, "One hundred views of Mount Fuji," written by one of the keepers of the British Museum and was published by the British Museum in this year of Britain–Japan collaboration. I think it is very fitting for this occasion. I hope you will enjoy this and you do not have any copy of the pictures in your home.

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Sasakawa Declaration in Moscow

The accident that occurred at the Chernobyl Nuclear Power Plant on the 26th of April 1986 will be remembered as an event which shook the world and awakened the consciousness of all people to the realization that a nuclear accident in one country could easily cross national boundaries and affect both distant and adjacent countries, and to an awareness of the more general issue of the safety of nuclear power plants.

One of the lingering problems of the Chernobyl accident is the concern regarding various health effects among the several populations directly affected by the accident, especially the emergency workers and people living in radiation-contaminated areas. Among the latter, there has been a dramatic increase in thyroid cancer among those who were children or adolescents at the time of the accident, the risk of which is expected to be long-lasting.

Now we have entered into the new century. With the introduction of the new concept of "environmentally sound sustainable development" and from the viewpoint of "protecting the human environment," we are required to review the consequences of this accident, to further clarify both radiation-induced and nonradiation-related late health effects and to assess and understand them for the future welfare of society.

Here we propose that the findings of the Chernobyl Sasakawa Health and Medical Co-operation Project, carried out in Belarus, Russia and Ukraine using a uniform protocol for the diagnosis and treatment of related health effects, and for associated research, be the bases for additional studies in the 21st century.

Based on the above, the international community is invited to participate in the effort to maintain the long-term follow-up of irradiated victims, to support field-oriented radiation research and to improve the health care of children and others affected by the Chernobyl accident.

31 May 2001

Drafted by:

Kenzo Kiikuni, Shigenobu Nagataki, Michael N. Repacholi, Guennadi N. Souchkevitch, Anatoly F. Tsyb, Bruce W. Wachholz, Shunichi Yamashita.

PII: S0531-5131(01)00848-2

Invited papers

International Congress Series 1234 (2002) 163–168

Iodine nutrition in the Chernobyl area before and after the nuclear accident

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Abstract

Reports from 1950 to 1960 suggest that goiter was frequent in the Chernobyl area and vigorous efforts were undertaken to distribute iodine supplements. There resulted enthusiastic reports stating that endemic goiter was no longer a problem. During the 1970s, the distribution of iodized salt became undependable and by 1980, goiter incidence was reported to have increased. Four to ten years after the Chernobyl nuclear accident, severe iodine deficiency was unusual but goiter by ultrasound measurement was found in more than 35% of the children. Unusual thyroid cancer appeared and its prevalence continues to increase. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Iodine; Goiter; Chernobyl; Thyroid

1. Introduction

Through the years, iodine nutrition has been evaluated chronically by the prevalence of enlarged thyroids [1] and acutely by urinary iodide excretion [2].

Following two devastating world wars in Europe, goiter surveys were conducted in the 1950s [3]. In the marshy areas, along the Pripet River between Belarus and Ukraine, 20% of the schoolchildren was found to have goiter. In 1956, an iodine map of Ukraine was published showing approximately 3 μg iodine per liter of ground water in the Chernobyl area [4]. Severe endemic goiter was reported in the mountainous areas of Southwestern Ukraine [5–7], but this was not the major fallout area of Chernobyl.

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PII: S0531-5131(01)00605-7

Mandatory iodination programs [8–10] were undertaken throughout the country with highly successful results [10,11]. In 1958, during the Fifth Five-Year Plan, the Ukrainian Institute of Experimental Endocrinology [7] set a goal to "liquidate goiter disease among children during the Sixth Five-Year Plan." By the 1970s, several regions of Ukraine were reported as having "no endemic goiter as a mass disease," and in Belarus, goiter was reported as "mild to moderate" [12]. However, in 1970, national programs to control iodine deficiency were discontinued [9,10]. During the 1980s, interest in the iodine supplementation programs were reduced [10,11], use of iodized salt was erratic, and free distribution of "antistruma" (potassium iodide) supplement was discontinued [8–10].

The prevalence of clinical goiter in the Chernobyl area was not known at the time of the Chernobyl accident in 1986. Russian authors [5,6,12] reported that early in 1980, the incidence of new cases of goiter began to increase and by 1990, goiter had exceeded its greatest number in 20 years in most of Belarus [5,6,12]. Information is unclear as to how iodine medication was administered in the area following the nuclear accident [13].

In nearby Poland, radioactive fallout was much less than in the Chernobyl area but 18–58% of the population had goiter and 18 million doses of potassium iodide prophylaxis were administered to more than 90% of children of Poland within 7 days after the Chernobyl accident [14]. The purpose of potassium iodide was to dilute the environmental radioiodine to reduce the fraction of radioiodine incorporated into thyroid glands.

In 1990, The International Chernobyl Project of the International Atomic Energy Agency used ultrasound to survey the thyroid glands of the residents in the Chernobyl area. They reported no unusual thyroid nodularity and did not comment upon finding endemic goiter [15].

2. Urinary iodide measurements

In the Chernobyl area, investigations of urinary iodine metabolism were not reported until after the first thyroid cancers were seen in 1990 and reported in 1991 [16]. The first measurements of urinary iodide were begun 4 to 5 years after the accident, when Astakhova et al. [17] measured urinary iodide in 393 schoolchildren of Belarus during 1990–1991. They found 56% of the samples contained less than 50 μg/l (moderate iodine deficiency), but 36% from 106 children of Vetka showed the measurements less than 20 μg/l (suggestive of severe iodine deficiency). In 1993, the same laboratory [18] studied 20785 subjects from Belarus and they found only 13% of 88 urine samples from Vetka contained less than 20 μg/l.[1] Those data suggest that in Vetka (Gomel), a severe iodine deficiency may have improved between the 4th and 7th year after the accident.

Parts of the data of Astakhova et al. [18] may have been included in a report by Mityukova et al. [19] regarding 1680 children, age 8–16 years, over a 3-year period. They showed an increased median urinary iodide in Vetka, from 36 to 68 μg/l between 1990 and 1993.

[1] Tabulated as mg/l, but referred to as μg/l in the accompanying text of Ref. [18].

Table 1
Classification of goiter endemias by severity

Variable	Target population	Mild IDD	Moderate IDD	Severe IDD
Prevalence of goiter (grade > 0) (%)	SAC	5.0–19.9	20–29.9	>30
Frequency of thyroid volume >97th centile by ultrasound (%)	SAC	5.0–19.9	20–29.9	>30
Median urinary iodine level (μg/l)	SAC	50–99	20–49	< 20

SAC = school age children; IDD = iodine deficiency disorders. Adapted from Ref. [21].

In Ukraine, there were no post-Chernobyl reports of urinary iodide, until 1991, when a pediatrician in Kiev [20] collected urine from 100 children in Kiev, Rovno, Zhitomir and Chernogov. The samples were preserved and sent to USA for iodine analyses. The data show a median of 50 μg/l, in this small sample of Ukrainian children, suggesting a moderate iodine deficiency in 1991–1992. Twelve percent of the subjects excreted less than 20 μg/l (compatible with severe iodine deficiency). Ten of the children were reported to have clinical goiter, three excreted more than 200 μg/l, and one excreted 16 000 μg/l, suggesting an occasional case of inappropriately high intake of iodine.

Delange [21] devised Table 1 to relate the severity of iodine deficiency to the prevalence of goiter and the daily urinary iodide. This tabulation has become a convenient index.

Improvements were made in the methods for measurement of iodide excretion [22] and an improved technique was introduced for the ultrasound measurements of thyroid size [23].

3. Measurement of thyroid size

Since the introduction of objective technology, the definition of goiter has changed. Previously, goiter was defined as a thyroid lobe, larger than the terminal phalanx of the thumb of the subject [24]. With modern ultrasound technology, a thyroid gland is termed as "goiter" when it is larger than the thyroids found in 97% of the normal population [25,26].

Ultrasound techniques differ among operators to such an extent that examiners must compare their results with each other and among controls, because the normal thyroid of children is small (2 to 15 g) and techniques may differ. Zimmermann et al. [27], in a recent consensus study, showed that the ultrasound measurements by WHO were 30% larger than those of some other operators.

Arinchin et al. [28] conducted a goiter survey in Belarus during 1995–1998, examining 11 562 children by ultrasound and palpation of the neck. Their results, compared to WHO standards, showed 17% goiter by ultrasound but 33% by palpation. Therefore, at present, ultrasound techniques may require inter-comparison of normal controls to insure quantitative agreement regarding the frequency of normal and abnormal thyroid sizes.

4. Sasakawa investigation of goiter and urinary iodide

In 1991, the Sasakawa Memorial Health Foundation [29] began intensive studies of the children in the Chernobyl area, which they continued for 5 years. Ashizawa et al. [30] reported the thyroid sizes from more than 119000 children in the Chernobyl area. They had found that the standard ultrasound methods underestimated the size of the thyroid, therefore, they calibrated their methods, using 800 normal children of the Mogilov Medical Diagnostic Center (one of the five health screening centers in the Chernobyl area). All of the "standard" subjects had adequate iodine intake, normal measurements of thyroid stimulating hormone, normal serum-free thyroxine and absence of antithyroid antibodies. The Sasakawa investigators carefully established a thyroid "limit" size, above which was defined as "goiter." To do this, they developed an exponential expression and calculated a thyroid volume related to age, height and weight [30]. They further calibrated their volume measurements by a computerized digitizer. In addition, they measured pre- and post-operative thyroid sizes from a series of thyroidectomies. The surgical subjects were mostly adults, and the operating surgeons estimated the volume of thyroid not removed [23].

Many goiters were discovered in the Chernobyl area [30]. The median thyroid sizes approached the P-97 values of the thyroid volumes reported by WHO from the schoolchildren of Eastern Europe [31] and further exceeded the thyroid volumes of European children reported by earlier investigators [32].

Goiter was found most frequently in children from Kiev, where 54% of 14800 children had goiter but their median iodide excretion was 82 μg/l urine [30]. Such iodide output is compatible with only mild iodine deficiency (Table 1). The results confirmed an earlier abstract [33], which was quoted [8,9] to have reported 32% to 56% goiter in adolescents from Kiev. These data suggest that iodine intake was only mildly deficient but a goiter frequency of 50% is a severe endemic. Therefore, there may have been an unidentified goitrogen in the community or iodine intake may have been only recently increased, such that the goiters may have been undergoing resolution.

5. Extremes of urinary iodide

The highest levels of iodide excretion around Chernobyl were 1000 to 10000 μg/l of urine, from children of Gomel, Mogilev, Bryansk, Kiev and Zhitomir. These values far exceeded the highest concentrations (600 μg/l) reported from the schoolchildren of Western Europe [31]. The extreme iodine intakes suggest that some children in the Chernobyl area may have ingested relatively large doses of iodine, which could have resulted in iodide thyroiditis [33–35].

6. Disparity between thyroid cancer and recent iodine metabolism

It is emphasized by Ashizawa et al. [30] that 5 to 10 years after the nuclear accident, the population of Gomel showed the least prevalence of goiter and the highest median iodine intake in the Chernobyl area and this was confirmed by Arinchin et al. [28]. If those conditions were true before and during the nuclear accident in 1986, Gomel might have been relatively protected from radioiodine fallout. However, the relatively high dose of radioiodine, from the Chernobyl accident, may have negated a potential protection. The result is that among the regions around Chernobyl, Gomel has supplied the largest number of cases of childhood thyroid cancer [36–38].

References

[1] O.P. Kimball, The prevention of simple goiter in man, Am. J. Med. Sci. 163 (1922) 634–649.

[2] J. Podoba, Endemicka Struma Na Slovensku, Slovenskej Akademie Vied, Bratislava, 1962.

[3] F.C. Kelly, W.W. Snedden, Prevalence and geographical distribution of endemic goitre, Bull. W. H. O. 18 (1–2) (1958) 5–173.

[4] S. Savchenko, An iodine map of the Ukrainian SSR, Dokl. Akad. Nauk SSR 108 (1956) 889–891.

[5] V.A. Oleynik, A.D. Bely, The problem of endemic goiter prophylaxis in the Ukraine, International Symposium, The Elimination of Iodine Deficiency Disorders, Tashkent, Uzbekistan, 1991, pp. 119–124.

[6] V.A. Oleynik, A.D. Bely, The problems of endemic goiter prophylaxis in Ukraine, IDD Newsl. 8 (1) (1992) 8.

[7] D.V.Ia. Aber, Endemic goiter disease in the Ukraine, Probl. Endokrinol. Gormonoter. 4 (2) (1958) 47–52 (in Russian), Translated (NIH-90-141) into English by Ted Crump for National Institute of Health Library, Behtesda, MD.

[8] G. Gerasimov, Update on IDD in the former USSR, IDD Newsl. 9 (4) (1993) 43–48.

[9] G. Gerasimov, O. Judenitch, I. Dedov, Iodine deficiency disorders and endemic goiter in the Commonwealth of Independent States (CIS), in: F. Delange, J.T. Dunn, D. Glinoer (Eds.), Iodine Deficiency in Europe: A Continuing Concern, Plenum, New York, 1993, pp. 347–351.

[10] I.I. Dedov, Endemic goiter in the former USSR: problems and solutions, IDD Newsl. 8 (1) (1992) 2.

[11] I.I. Dedov, Endemic goiter in the former USSR: problems and solutions, International symposium, The Elimination of Iodine Deficiency Disorders, Tashkent, Uzbekistan, 1991, pp. 25–34.

[12] E.A. Kholodova, L.P. Fedorova, Epidemiology of endemic goiter in Belarus, IDD Newsl. 8 (1) (1992) 3.

[13] Y.I. Gavrilin, V.T. Khrouch, S.M. Shinkarev, N.A. Krysenko, A.M. Skryabin, A. Bouville, L.R. Anspaugh, Chernobyl accident: reconstruction of thyroid dose for inhabitants of the Republic of Belarus, Health Phys. 76 (2) (1999) 105–119.

[14] J. Nauman, J. Wolff, Iodide prophylaxis in Poland after the Chernobyl reactor accident: benefits and risks, Am. J. Med. 94 (1993) 524–532.

[15] F.A. Mettler Jr., M.R. Williamson, H.D. Royal, J.R. Hurley, F. Khafagi, M.C. Sheppard, V. Beral, G. Reeves, E.L. Saenger, N. Yokoyama, V. Parshin, E.A. Griaznova, M. Taranenko, V. Chesin, A. Cheban, Thyroid nodules in the population living around Chernobyl, JAMA, J. Am Med. Assoc. 268 (5) (1992) 1–4.

[16] A. Prisyazhiuk, O.A. Pjatak, V.A. Buzanov, G.K. Reeves, V. Beral, Cancer in the Ukraine, post-Chernobyl, Lancet 338 (1991) 1325–1334.

[17] L.N. Astakhova, T.A. Mityukova, V.F. Kobzev, T.A. Luchenok, Investigation of endogenic deficiency of iodine in children and teenagers of endogenic regions of the republic, Zdravookhr. Beloruss. 2 (1993) 8–11 (in Russian).

[18] L.N. Astakhova, T.A. Mityukova, V.F. Kobzev, Endemic goiter in Belarus following the accident at the Chernobyl nuclear power plant, in: S. Nagataki, S. Yamashita (Eds.), Nagasaki Symposium Radiation and Human Health, Elsevier, Amsterdam, 1996, pp. 67–95.

[19] T.A. Mityukova, L.N. Astakhova, L.D. Asenchyk, M.M. Orlov, L. VanMiddlesworth, Urinary iodine excretion in Belarus children, Eur. J. Endocrinol. 133 (1995) 216–217.

[20] E.V. Bolshova, N.D. Tronko, L. VanMiddlesworth, Iodine deficiency in Ukraine, Acta Endocrinol. 129 (1993) 594.

[21] F.M. Delange, Iodine deficiency, in: L.E. Braverman, R.D. Utiger (Eds.), Werner and Ingbar's The Thyroid, Lippincott Williams and Wilkins, 530 Walnut St. Philadelphia, PA 19106, 2000, p. 296, Table 13.11.

[22] K. Tsuda, H. Namba, T. Nomura, N. Yokoyama, S. Yamashita, M. Izumi, S. Nagataki, Automated measurement of urinary iodine with use of ultraviolet irradiation, Clin. Chem. 41 (4) (1995) 581–585.
[23] N. Yokoyama, Y. Nagayama, F. Kakezono, T. Kiriyama, S. Morita, S. Ohtakara, S. Okamoto, I. Morimoto, M. Izumi, N. Ishikawa, K. Ito, S. Nagataki, Determination of the volume of the thyroid gland by a high resolutional ultrasonic scanner, J. Nucl. Med. 27 (9) (1986) 1475–1479.
[24] C. Perez, N.S. Scrimshaw, J.A. Munoz, Technique of endemic goiter surveys, Endemic Goiter, Monograph Series, vol. 44, WHO, Geneva, 1960, p. 369.
[25] World Health Organization and International Council for Control of Iodine deficiency Disorders, Recommended normative values for thyroid volume in children aged 6–15 years, Geneva: Nutrition Unit, WHO, Reprint # 5757, Bull. W. H. O. 75 (2) (1997) 95–97.
[26] F. Delange, What do we call a goiter? Eur. J. Endocrinol. 140 (1999) 486–488.
[27] M.B. Zimmermann, L. Molinari, M. Spehl, J. Weidinger-Toth, J. Podoba, S. Hess, F. Delange, Toward a consensus on reference values for thyroid volume in iodine-replete schoolchildren: results of a workshop on interobserver and inter-equipment variation in sonographic measurement of thyroid volume, Eur. J. Endocrinol. 144 (2001) 213–220.
[28] A. Arinchin, M. Gembicki, K. Moschik, A. Skalyzhenko, I. Khmara, N. Korytko, S. Petrenko, N. Gomolko, V. Balakleevskaya, S. Laptenok, R. Bertollini, Goiter prevalence and urinary iodine excretion in Belarus children born after the Chernobyl accident, IDD Newsl. 16 (1) (2000) 7–9.
[29] Sasakawa Medical Symposium, In: S. Yamashita, Y. Shibata (Eds.), Chernobyl: A Decade, Elsevier, PO Box 211, 1000 AE, Amsterdam, The Netherlands, 1997.
[30] K. Ashizawa, Y. Shibata, S. Yamashita, H. Namba, M. Hoshi, N. Yokoyama, M. Izumi, S. Nagataki, Prevalence of goiter and urinary iodine excretion levels in children around Chernobyl, J. Clin. Endocrinol. Metab. 82 (10) (1997) 3430–3433.
[31] F. Delange, G. Benker, Ph. Caron, O. Eber, W. Ott, F. Peter, J. Podoba, M. Simescu, Z. Szybinsky, F. Vertongen, P. Vitti, W. Wiersinga, V. Zamrazil, Thyroid volume and urinary iodine in European schoolchildren: standardization of values for assessment of iodine deficiency, Eur. J. Endocrinol. 136 (1997) 180–187.
[32] R. Gutekunst, H. Martin-Teichert, Requirements for goiter surveys and the determination of thyroid size, in: F. Delange, J.T. Dunn, D. Glinoer (Eds.), Iodine Deficiency in Europe: A Continuing Concern, Plenum, New York, 1993, pp. 109–122.
[33] A. Smirnov, Prevalence of thyroid hyperplasia in children in Kiev 1989, Third All Union Endocrinology Congress, 1989, pp. 564 (in Russian).
[34] M.A. Boukis, D.A. Koutras, A. Souvatzoglou, A. Evangelopoulou, M. Vrontakis, S.D. Moulopoulos, Thyroid hormone and immunological studies in endemic goiter, J. Clin. Endocrinol. Metab. 57 (4) (1983) 859–862.
[35] G.J. Kahaly, H.P. Dienes, J. Beyer, G. Hommel, Iodide induces thyroid autoimmunity in patients with endemic goitre: a randomized, double-blind, placebo-controlled trial, Eur. J. Endocrinol. 139 (1998) 290–297.
[36] D. Bard, P. Verger, P. Hubert, Chernobyl, 10 years after: health consequences, Epidemiol. Rev. 19 (2) (1997) 187–204.
[37] E. Demidchik, A. Mrochek, Y. Demidchik, T. Vorontsova, E. Cherstvoy, J. Kenigsberg, V. Rebeko, A. Sugenoya, Thyroid cancer promoted by radiation in young people of Belarus (clinical and epidemiological features), in: G.A. Thomas, et al. (Eds.), Radiation and Thyroid Cancer, World Scientific, Singapore, 1999, pp. 51–54.
[38] R. Stone, Living in the shadow of Chernobyl, Science 292 (5516) (2001) 420–426.

International Congress Series 1234 (2002) 169–174

Implementation of WHO's guidelines for iodine prophylaxis following nuclear accidents: Update 1999

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Abstract

In December 1999, WHO issued an update to their guidelines on the use of stable iodine as a prophylactic measure to protect the thyroid gland from radioiodine, issued in 1989. The present paper explains the need for the update and discusses how the revised recommendations are implemented in practice. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Iodine-prophylactic use; Thyroid gland; Nuclear reactors; Accidents; Guidelines

1. History of WHO guidelines on stable iodine prophylaxis

Following the nuclear power plant (NPP) accident at Chernobyl in Ukraine in 1986, the WHO Regional Office for Europe (WHO/EURO) reviewed, in detail, the evidence concerning the effectiveness and safety of using blocking agents to prevent the uptake of radioactive iodine to the thyroid. At that time, the evidence indicated that provided stable iodine, in the form of potassium iodate or iodide, was taken either before or shortly after exposure commenced, 100 mg of stable iodine (in the adult, proportionately less in children) would be effective in blocking the uptake of radioactive iodine for periods in the order of 24 h. Although such administrations were thought to be safe, there was no data from which to assess the risks in a large population.

In 1989, WHO/EURO issued guidelines [1] for the use of stable iodine in what was then called the "near field" and would now be termed the emergency planning zone (EPZ), an area extending from 5 to 10 km from the site of the release of radioactivity. The decision on whether to issue the tablets would be a matter for the local authorities concerned with the

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PII: S0531-5131(02)00162-0

NPP that was either about to release, or releasing, radioactive iodine. A single administration was anticipated as the primary hazard was seen as being due to the inhalation of iodine in air, and this exposure would be of limited duration since in the case of a prolonged release, evacuation of the near field would be undertaken.

2. Evidence accruing from the Chernobyl accident

At about the same time as the above guidelines were issued, it is now clear that the first cases of childhood thyroid cancer in Belarus were appearing. By 1991, reports by Belarussian doctors were being made at scientific meetings claiming significant increases in childhood thyroid cancer, normally a very rare disease. Early in 1992, a WHO expert group, convened in collaboration with the EU, examined the evidence and concluded that further investigation was warranted. In July 1992, a visit to Minsk by a small team of experts under the auspices of WHO/EURO, in collaboration with Belarussian doctors, reported a significant increase in childhood thyroid cancer [2]; as a result, the WHO International Thyroid Project, which was designed to assist Belarus in addressing the increase in disease, was initiated.

As the extent and magnitude of the increase in thyroid cancer became clear over the following years, it was realized that the sensitivity to the induction of thyroid cancer must be very high in children. There was considerable skepticism in the global scientific community that the increase was associated with the accident. If it were, the most probable agent responsible was ^{131}I, an isotope widely used in diagnosis and treatment of thyroid disease and thought to have a very low capacity to induce cancer. Much effort was expended in trying to determine whether the increase was related to the accident or was, for example, an artifact resulting from increased screening of children.

By 1995, few skeptics remained, as relative risks (the ratio between the observed incidence rate and the expected rate) were in the order of between 1 and 200 in some districts, particularly the Gomel Region, in southeastern Belarus, the closest part of the country to the site of the accident, but still extending to more than 200 km from the NPP. However, incidence rates were also markedly increased in places several hundred kilometers from the site of the accident. It was clear that these increases were not the result of inhalation of radioactive iodine, but of drinking contaminated milk. As the half-life of ^{131}I is 8 days, most of the radioactivity decays within a few months, but during that period, there could be continued exposures, especially where fresh milk is a staple of the diet.

This experience cast a clear question mark over a number of features of the then existing guidelines; and in 1996, WHO took steps to review those guidelines in the light of the experience from the Chernobyl accident.

3. Experience in the distribution of stable iodine in Poland

Immediately following the accident, with the wind carrying fallout over southern Belarus and northern Ukraine, towards Poland, the Polish public health authorities initiated a mass distribution of stable iodine, for children (10.5 million administrations). In addition, 7 million adults took iodine although it was not recommended. Tablets were not available, so potassium iodide solution was used.

Subsequent follow up of this population [3,4] revealed few serious adverse reactions to the administration, two in adults but none in children. This published information provides a secure basis for estimating the risk of administered stable iodine. The risk for serious side effects, per administration, can be assessed at 1 in 10^7 children, and 1 in 10^6 adults.

4. The scientific basis for estimating the risk of exposure to ^{131}I

Early animal experiments (mainly using rats) appeared to indicate that ^{131}I was not as carcinogenic as X-rays delivered from an external source to the thyroid [5]. However, it would appear that this was due to the use of insufficient numbers of animals; and in 1982, a much more comprehensive experiment was reported indicating no differential effect between X-rays and ^{131}I [6]. ^{131}I has also been in use both as a diagnostic and therapeutic agent for thyroid disease and, particularly in Europe, extensive epidemiological follow up of patients was available. These studies reported no excess of thyroid cancer whereas more limited studies, in terms of numbers, mainly on children exposed to external X-rays, show a marked sensitivity to the induction of thyroid cancer.

This apparent paradox was resolved with a meta-analysis of five cohort studies of populations exposed to external X-rays [7], which revealed a marked age dependence of sensitivity to the induction of thyroid cancer, in terms of excess relative risk (ERR), with the youngest children being at greatest risk. The lack of children in the studies of the diagnostic use of ^{131}I and ablation of the thyroid tissue in the therapeutic use of ^{131}I explain the absence of excess thyroid cancer in these study populations.

Thus, the marked, particularly in terms of relative risk, increase in thyroid cancer in the children living in southern Belarus is not surprising. In respect of protecting a population against an environmentally caused disease, however, ERR is not the most appropriate indicator of effect. More relevant is excess absolute risk (EAR), that is, the total number of cases caused by a unit of exposure, independent of the spontaneous rate of appearance of the disease. EAR does not fall off as rapidly with increasing age at exposure as does ERR, as the spontaneous incidence rate of childhood thyroid cancer also increases sharply with increasing age. Studies on the populations living in southern Belarus and northern Ukraine indicate that EAR, in relation to the absorbed thyroid dose, is not significantly different for ^{131}I compared to externally generated X-rays, although the median risk is generally somewhat lower for the ^{131}I [8].

5. Preparation of the "Update 1999"

With the clear indications of the safety of stable iodine from the Polish experience, particularly in the young, and of the sensitivity of the young to the carcinogenic effects of radiation in general and ^{131}I in particular, it seemed appropriate to revise the 1989 guidelines on the use of stable iodine after nuclear accidents. Two features of the experience gained from the Chernobyl accident were relevant, namely, the wide geographical distribution of the cases and the number of cases diagnosed particularly in the very young at the time of exposure.

In the revised guidelines, "Update 1999" [9], the terms near and far field are dropped and it is recognized that stable iodine can be used to protect against ingested, as well as inhaled radioiodine, at least in the early stages of an exposure.

The strong age dependence of the induction of thyroid cancer by radiation needs to be addressed in any public health policy related to radioiodine. The mass distribution of a drug (as potassium iodide and iodate are defined in some countries) albeit of demonstrated safety, should not be treated lightly. The "Update 1999" thus seeks to target stable iodine prophylaxis to those whom it will be most effective and away from those whom it could present a hazard. Interventions to limit exposure in accident situations are determined on the basis of the extent to which dose can be averted by a particular interventional action [10]. The International Commission for Radiological Protection (ICRP) and the Basic Safety Standards of the International Agencies (BSS) provide so-called "generic intervention levels" (GILs), which provide a basis for planning interventions. In the event of an accident, interventions should be "optimized" to achieve a net benefit in terms of averted dose, social and economic costs being included in the cost–benefit analysis. This latter stipulation means that intervention policy will depend on circumstances peculiar to individual countries, therefore no intervention level as such could be recommended from an international point of view. However, WHO considered that some guidance could be provided on the interpretation of GILs through the use of "reference levels".

By comparing the incidence of serious side effects of stable iodine administration (about 1 in 10^7 per administration in childhood) with the serious consequences of exposure to radioiodine, namely cancer (for the youngest about 3% per Gy for boys and 6% per Gy for girls [11]), a "break even point" is attained at less than 0.01 mGy absorbed dose to the thyroid. It can, therefore, be concluded that any practical intervention has an overall health benefit for the young and WHO has recommended a reference level of 10 mGy, or one-tenth of the GIL for children and adolescents. Evidence from the Japanese atomic bomb survivors indicates that the risk in adults is low and probably nonexistent in those over 40 years of age. Therefore, the reference level for adults under 40 years is 100 mGy, equal to the GIL, but for older adults intervention is based on the deterministic limit of 5 Gy for the thyroid, as the stochastic risk is taken to be zero and the adverse side effects of stable iodine are likely to be more prevalent.

6. Experience with implementation

A workshop held by WHO [12], in collaboration with the Finnish Radiation and Nuclear Authority, in September 2000 discussed the implementation of the revised guidelines. The following are some of the issues raised at the workshop.

6.1. Timely distribution of stable iodine

For stable iodine to be effective, it must be administered just before or as soon after exposure commences as possible. This means, in practice, that decisions will be taken on projected doses as distribution takes time. This makes the concept of intervention levels almost redundant, as in practice, as soon as a release seems probable, a decision to issue stable iodine will be taken. Reconsideration should therefore be given to the criteria for intervention, possibly basing them preemptively on the probability of significant release according to reactor condition, rather than averted dose.

A number of innovative ideas to ensure timely availability of stable iodine to the most critical groups, namely young children, were discussed. The issuing of tablets to each newborn with their "passport" for medical follow up and social security benefits was one of the most effective actions.

6.2. The deterministic limit for adults over 40 years of age

A dose of 5 Gy was considered by many to be too high as an intervention for the elderly. During the preparation of the "Update 1999", a value of 1 Gy was initially proposed, but to achieve conformity with the BSS, 5 Gy was finally chosen. The evidence base for the deterministic limit of 5 Gy for the thyroid in the BSS should be reexamined.

6.3. Guidance to health care professionals

WHO was encouraged to produce "fact sheets" for nurses, doctors, hospital administrators, etc. to increase the general knowledge on issues related to nuclear accidents as a means of allaying unnecessary public concern.

7. Conclusions

Many countries now accept the need to revise their strategy in connection with the protection of the thyroid from radioactive iodine in the light of the experience gained from the Chernobyl accident. Stable iodine prophylaxis is a powerful means to do so over a relatively short period, but the unknown risks associated with repeated administration preclude the use of the method for protection against the entire period of exposure to ingested radioiodine following a deposition. The method is thus ideally used in conjunction with other mitigation measures such as removing cattle from contaminated pasture or controls on milk consumption in these circumstances.

The very rapid transfer of radioiodine to the thyroid, once it is internalized, means that any control measure has to be implemented rapidly, and for iodine prophylaxis, this is particularly important. Preemptive action is ideal, and for populations close to the source, this means deciding to implement prophylaxis before the release of radioactivity occurs; that is, based on the reactor condition and the probability and anticipated severity of release rather than any measure of exposure. In this case, intervention doses are redundant. However, at greater distances where several hours can elapse before deposition occurs, the reference levels of dose recommended (modified by any national considerations) can be used.

Iodine prophylaxis falls into the category of intervention measures that are expensive to adopt in terms of planning but cheap to implement in the event of an accident. This is in contrast to, for example, agricultural and food controls, which cost little to plan for but incur cost when they are implemented. In terms of public confidence in measures to protect public health, the acquisition of iodine tablets provides a more tangible proof than merely planning statements to the effect that in "such and such a circumstance the following actions will be taken." The investment may therefore be seen as having dual benefits.

References

[1] WHO, Guidelines for Iodine Prophylaxis Following Nuclear Accidents, WHO Regional Office for Europe, Copenhagen, 1989.

[2] V.S. Kazakov, E.P. Demidchik, L.N. Astakhova, K. Baverstock, B. Egloff, A. Pinchera, C. Ruchti, D. Williams, Thyroid cancer after Chernobyl, Nature 359 (6390) (1992) 21–22.

[3] J. Nauman, J. Wolff, Iodide prophylaxis in Poland after the Chernobyl reactor accident: benefits and risks, Am. J. Med. 94 (5) (1993) 524–532.

[4] J.A. Naumann, Practical experience of prophylaxis for large scale exposure after a nuclear accident, in: G. Thomas, A. Karaoglou, E.D. Williams (Eds.), Radiation and Thyroid Cancer, World Scientific, Cambridge, 1998, pp. 377–385.

[5] H.D. Royal, Relative biological effectiveness of external radiation vs. ^{131}I: a review of animal data, in: G. Thomas, A. Karaoglou, E.D. Williams (Eds.), Radiation and Thyroid Cancer, World Scientific, Cambridge, 1998, pp. 201–207.

[6] W. Lee, R.P. Chiacchierini, B. Shleien, N.C. Telles, Thyroid tumors following ^{131}I or localized X irradiation to the thyroid and pituitary glands in rats, Radiat. Res. 92 (2) (1982) 307–319.

[7] E. Ron, J.H. Lubin, R.E. Shore, Thyroid cancer after exposure to external radiation: a pooled analysis of seven studies, Radiat. Res. 141 (3) (1995) 259–277.

[8] P. Jacob, Y. Kenigsberg, G. Goulko, E. Buglova, F. Gering, A. Golovneva, J. Kruk, E.P. Demidchik, Thyroid cancer risk in Belarus after the Chernobyl accident: comparison with external exposures, Radiat. Environ. Biophys. 39 (2000) 25–31.

[9] WHO, Guidelines for Iodine Prophylaxis after Nuclear Accidents, Update 1999, WHO, Geneva, 1999.

[10] IAEA, International basic safety standards for protection against ionizing radiation and for the safety of radiation sources, Safety Series No., vol. 115, IAEA, Vienna, 1996.

[11] X. Xue, R.E. Shore, Assessing excess lifetime risk for disease after radiation exposure, Health Phys. 80 (5) (2001) 462–469.

[12] WHO, Workshop on Stable Iodine Prophylaxis after Nuclear Accidents, WHO Regional Office for Europe, Copenhagen, 2001(in press).

International Congress Series 1234 (2002) 175–183

Thyroid diseases around Chernobyl: from autoimmune diseases to malignant tumors

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Abstract

Both an increased incidence of thyroid carcinoma mainly of the papillary histotype and to a lesser extent, of autoimmune phenomena have been observed, several years after external irradiation to the head and the neck, in subjects treated for various non-thyroidal disorders, in atomic bomb survivors in Japan, and in residents of the Marshall Island exposed to radiation during the testing of hydrogen bombs. More recently, the exposure to radioactive fallout as a result of the Chernobyl nuclear reactor accident has clearly confirmed the causal association of radiation exposure and the development of thyroid autoimmune phenomena in the population exposed to radiation. This article will review the most significant features of thyroid diseases associated with the post-Chernobyl radioactive contamination. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Thyroid cancer; Radiation; Chernobyl; Autoimmune thyroid disease

1. Introduction

The thyroid gland is particularly sensitive to the effect of radiation and the evidence that radiation may damage the thyroid gland is overwhelming. Both external and internal radiation have been associated with thyroid diseases (cancer and hypothyroidism with or without thyroid autoimmunity) both in vitro and in vivo. In particular, ionizing radiation is recognized as the main risk factor for developing thyroid carcinoma especially when radiation exposure occurs during childhood [1].

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PII: S0531-5131(01)00606-9

A strong causal relationship has been demonstrated between papillary thyroid carcinoma and external irradiation to the head and the neck for various benign and malignant non-thyroidal disorders [2–5]. An increased risk of thyroid cancer has also been reported in survivors of the atomic bombs in Japan, as well as in Marshall Island residents exposed to radiation during the testing of hydrogen bombs [6,7].

The Chernobyl nuclear reactor accident has clearly caused an enormous increase in the incidence of childhood thyroid carcinoma in Belarus, Ukraine, and to a lesser extent, in the Russian Federation, starting in 1990 and continuing up to now. When epidemiological and clinical features of thyroid carcinomas diagnosed in Belarus after the Chernobyl accident are compared with those of naturally occurring thyroid carcinomas in patients of the same age group in Western European countries, it becomes apparent that the post-Chernobyl thyroid carcinomas were much less influenced by gender, were virtually always papillary (solid and follicular variants), had high aggressiveness at presentation, and were more frequently associated with thyroid autoimmunity [8,9].

Gene rearrangements, involving the RET proto-oncogene (less frequently TRK), have been demonstrated as causative event specific for papillary cancer. RET activation has been found in nearly 70% of the patients who developed papillary thyroid carcinomas following the Chernobyl accident, with specific peculiarities in respect with naturally occurring tumors.

In addition to thyroid cancer, radiation-induced thyroid diseases including benign thyroid nodules, non-autoimmune hypothyroidism, and autoimmune thyroiditis have been observed after environmental exposure to radioisotopes of iodine and in the survivors of atomic bomb explosion. In the population exposed to the post-Chernobyl radioactive fallout, thyroid autoimmune phenomena have been searched for in two studies in Belarus [10,11]. The result of these studies demonstrated an increased prevalence of circulating thyroid antibodies not associated with significant thyroid dysfunction. This is in keeping with the short period of follow-up, but the possibility of later development of clinical thyroid autoimmune diseases especially hypothyroidism is very likely. Future screening programs for thyroid diseases in the population at risk should be focused not only on the detection of thyroid nodules and cancer, but also on the development of thyroid autoimmune diseases.

2. The thyroid gland as a specific target for radiation-induced damage

In April 1986, the explosion of one of the reactors at the nuclear power plant in Chernobyl (Ukraine) released large amounts of radioactive particles into the atmosphere, including I-131 (32–46 MCi), I-132 (27 MCi; resulting from the decay of Tc-132) and I-133 (68 MCi). Most likely, radioiodines were released intermittently over a period of 10 days after the accident. The most contaminated territories were southern Belarus, northern Ukraine, and the Bryansk and Kaluga regions of southwestern Russia.

In case of radioactive contamination, the thyroid gland is a critical organ at risk. Its contamination depends upon the magnitude of contamination, the amount of radioactive iodine taken up by the gland and the thyroid mass itself. Furthermore, whatever the level of contamination, the thyroid dose is always higher in children than in adults. The thyroid dose is dependent from the final concentration, namely the ratio between radioiodine uptake and thyroid mass. In children, the uptake is similar to adults but since the thyroid mass is smaller, the thyroid dose per gram of tissue is greater and extremely higher in newborns and very young children. In the Chernobyl case, radioactive isotopes of iodine represent a high proportion of the contaminating isotopes.

Being volatile, radioactive isotopes are firstly inhaled and, after being deposited on the ground, ingested. The time at which ingestion occurs varies considerably but the milk chain, particularly in children, is the major route of ingestion; at this time, short-lived isotopes of iodine are no longer present. In the Chernobyl accident, several factors contributed to the high radiation exposure of the population. Immediate protective countermeasures such as advising and evacuating the people at risk and distributing iodine prophylaxis were not undertaken. Furthermore, the most contaminated regions were in a state of moderate iodine deficiency, which is responsible for increased iodine uptake. All these factors combined give enough explanation of why the most serious health consequences of the disaster affected the thyroid gland, and why children were mostly affected.

3. Post-Chernobyl thyroid cancer

3.1. Epidemiology

As a result of the accident, a tremendous increase in the number of childhood papillary thyroid cancer has occurred in the following years, continuing up to now [12–14]. The magnitude of this increase and the geographical and temporal distribution of the cases strongly suggest that thyroid cancer was due to the reactor explosion, and in particular, to the huge amount of iodine radioisotopes released [15]. The increase in the number of thyroid carcinoma in children and adolescents has been observed starting from 1990, only 4 years after the Chernobyl accident, in southern Belarus and northern Ukraine, and from 1994 in southwestern Russia [16–19].

To date, more than 1000 cases of thyroid cancer have been reported among approximately 2 million children younger than 15 years, who were exposed to radioactive fallout. In the Gomel region, the most contaminated area of Belarus, the incidence between 1986 and 1996 was 13 per 100 000 children per year compared to a baseline incidence of less than one per year [20]. About 98% of these thyroid tumors have been observed in children less than 10 years of age and 65% in children less than 5 years at the time of the accident. Thyroid cancer was also diagnosed in some children who were already generated but still in the uterus at the time of the accident. An increased incidence is now observed also in adolescents and adults.

The annual distribution of new cases of thyroid cancer shows that the increase in children reached its peak in 1993, with a trend to a "plateau" in the following years [8]. It is also apparent that the patients of the 5-year or less age group at the time of the accident accounted for the majority of the cases in each year of observation. In contrast, a decreasing number of thyroid cancer cases was observed in patients who were 9 years of age or older at the time of the accident, with no new cases being observed in 1995.

The mean latent period between radiation exposure and diagnosis is about 9–10 years, with a similar trend in children and adolescents, shorter than that found after external thyroid irradiation [3,4].

3.2. Genetics

Molecular biology investigation of post-Chernobyl tumors shows some peculiarities. *Ras* and *p53* genes are not involved in their pathogenesis. Rearrangements of the RET proto-oncogene are found in nearly 70% of the cases, a percentage higher than that observed in naturally occurring papillary carcinomas [21–24]. Also, the subtype of RET/PTC rearrangement has a peculiar pattern. Several authors have reported that RET/PTC3 (and more rare variants of RET/PTC3) is the form more frequently expressed in radiation-induced tumors, rather than RET/PTC1, which is predominant in naturally occurring cases [25]. A correlation has also been established between the solid variant of papillary tumors and the activation of RET/PTC3 [24].

These data indicate that RET/PTC activation may be the direct result of radiation-induced DNA damage. Since RET/PTC is also frequently found in pediatric papillary thyroid cancer without known exposure to radiation, it is also possible that age per se may play an important role. Alternatively, one can speculate that virtually all pediatric papillary thyroid cancers are radiation-induced cancers, developing in subjects with an increased susceptibility to spontaneous background radiation [26].

3.3. Comparison with naturally occurring tumors

A comparison between clinical and epidemiological features of thyroid carcinomas diagnosed in Belarus after the Chernobyl accident and those of 369 children and adolescents, followed in the past 20 years for thyroid carcinoma in Italy and in France, shows that the post-Chernobyl thyroid carcinomas were much less influenced by gender, the female to male ratio being significantly higher in Italy and in France (2.5:1) compared with Belarus patients (1.6:1). Similar findings have been found in the series from England and Wales [9]. Furthermore, most of the patients in Belarus (87.9%) were diagnosed before the age of 15 years, while the number of cases in Italy and in France increased progressively with age, with the majority of the patients (57.4%) being diagnosed after the age of 14 years [8].

Over 90% of the post-Chernobyl childhood thyroid carcinomas were papillary, very few being of the follicular histotype [8,27]. Only a minority (about 10%) were of the classic papillary histologic type; most cancer (33%) were of the solid and follicular variants. The diffuse sclerosing variant accounted for roughly 10% of these carcinomas [28]. The histological features were those of aggressive tumors, as demonstrated by their histologic appearance, the large size and the frequency of multifocality, extracapsular extension, lymph node metastases, and lung metastases at the time of diagnosis [29]. A comparison with naturally occurring thyroid carcinomas in Italy and France showed a significantly higher extrathyroidal extension in Belarus children (49.1%) with respect to age-matched cases in Italy and France (24.9%) [8]. A high frequent association of post-Chernobyl tumors with lymphocyte infiltration of the thyroid gland and humoral thyroid autoimmunity has also been reported [8].

3.4. Response to conventional treatment

Radioiodine therapy is a safe and useful procedure for the postsurgical ablation of thyroid residues [30]. Usually, a single treatment is sufficient to achieve complete thyroid ablation in 65–90% of the cases, but a significant proportion of patients may require additional treatment [31].

A recent study [32] reports the results of postsurgical radioiodine thyroid ablation in 249 Ukrainian children and adolescents with post-Chernobyl-differentiated thyroid cancer, initially treated with near-total thyroidectomy. Radioiodine scan performed 6–8 weeks after surgery revealed the presence of residual thyroid tissue in all cases. All patients received one or more courses of radioiodine therapy for a total of 468 courses. Only 129/249 patients (51.8%) were ablated and among them, only 63 were ablated with a single dose of radioiodine. These results indicate that in this particular population of post-Chernobyl thyroid carcinomas, thyroid ablation is a rather difficult task. Possible explanation for this finding may be the young age of the patients, other particular features of post-Chernobyl thyroid carcinoma or technical aspects, such as less radical surgery procedures.

Another study [33] analyzed the outcome of 64 Belarus children with post-Chernobyl papillary thyroid carcinoma who received postsurgical treatment and follow-up in Pisa. Initial treatment consisted of total thyroidectomy in all patients, followed by I-131 therapy for ablation of any thyroid residue and/or for treatment of functioning local or distant metastases and L-thyroxine-suppressive therapy. The result of treatment was analyzed according to serum thyroglobulin levels and results of I-131 whole body scan. After a mean follow-up of 38.6±25.8 months, 33 (58.9%) patients were free of disease and 23 (37.5%) had persistent disease, including 14 lymph node metastases and seven with lung metastases. Two patients (3.5%) developed lung metastases during follow-up. The results of this study indicate that patients with radiation-induced papillary thyroid carcinoma treated with the combination of surgery, radioiodine, and hormonal therapy have a successful response to treatment not different from that observed in age-matched series of patients with naturally occurring thyroid carcinoma.

4. Post-Chernobyl thyroid autoimmunity

Thyroid cancer and benign thyroid nodules after thyroid radiation exposure occur as stochastic effects. Depending on the radiation dose, deterministic effects, hypothyroidism, and acute thyroiditis are also possible. Another documented consequence of radiation is the possibility of developing autoimmune thyroid disorders.

Hypothyroidism is caused by radiation doses of the order of more than several gray to the thyroid. Such levels are mainly observed after radioiodine therapy for benign thyroid diseases, such as Graves' disease and toxic nodular goiter, and in this case hypothyroidism is the objective of treatment.

Spontaneous hypothyroidism (or subclinical hypothyroidism) has been reported in survivors of atomic bomb in Nagasaki [6]. After external irradiation to the head and neck, the occurrence of thyroid autoimmunity has been reported in several studies. An increased incidence of thyroid antibodies was found by De Groot et al. [34] in subjects who received radiation during childhood for benign disorders. Variable degree of thyroid lymphocytic infiltration have been reported in more than two thirds of individuals who received radiation several years before thyroidectomy for nodular thyroid lesions [35]. In patients who received radiation of the neck for Hodgkin's disease, 3% or more developed Graves' disease (a 7–20-fold excess risk) and 1% thyroiditis [5].

Hypothyroidism has also been reported after exposure to internal radiation (radioactive iodine). In the people exposed to the fallout of the Marshall Islands accident [7], hypothyroidism was noted within 10 years from the accident. In this occasion, most of the cases were not associated to autoimmune thyroid reaction.

On the contrary, an increased prevalence of antithyroid antibodies without hypothyroidism has been reported in children living in Belarus village, which is heavily contaminated by the post-Chernobyl radioactive fallout, as opposed to children living in a noncontaminated village. In particular, in a recent study [10], the authors evaluated thyroid autoimmune phenomena in 287 (9.2%) of the 3105 children (age at accident, 0–9 years) from the village of Hoiniki south of Gomel, which was contaminated by the post-Chernobyl radioactive fallout (5.4 Ci/km^2 of cesium). The control group consisted of 208 (3.9%) of the 5273 children of the same age from Braslav in the region of Vitebsk, which was not contaminated (<0.1 Ci/km^2). In all patients, thyroid function was assessed by measuring serum TSH, free T_3 and T_4, and humoral thyroid autoantibodies (antithyroglobulin and antithyroperoxidase). The prevalence of antithyroglobulin or antithyroperoxidase, or both, was significantly higher (p=0.0001) in children living in Hoiniki (19.5%) than those living in Braslav (3.8%). In both villages, no sex differences were found in the antibody prevalence before age 13 years; thereafter, a significantly higher prevalence of thyroid autoantibodies was found in girls from Hoiniki. The prevalence of circulating antibodies in the contaminated group started to increase in children who, at the time of the accident, were in utero or newborns (15.7%), plateaued until age 8 years and showed a further increase in children 8–9 years of age (30.1%). In the control group, a very modest prevalence of positive antibodies was found, starting in the second year of life and remaining constant thereafter. No major alterations of serum-free T_4, free T_3, or TSH were found. In conclusion, the susceptibility to develop thyroid autoimmunity increased with age at the time of exposure and, in the female sex, reached its maximum in the pubertal age, suggesting that puberty (estrogen) has an accumulative effect on radiation in the development of thyroid antibodies in females. This study was conducted only 6–8 years after the Chernobyl accident, which may be the reason why cases of overt hypothyroidism were not found. However, the possibility of later development of thyroid failure is very likely in this population.

These data have been confirmed in a similar study [11], which was carried out in Russian children and adolescents living in the district of the Tula region that has moderate iodine deficiency and low Cs-137 contamination. The authors demonstrated a high prevalence of positive thyroid antibodies in children and adolescents already born or in utero at the moment of the nuclear accident. A much lower prevalence, almost identical to the prevalence registered in uncontaminated area, was found in children conceived and born 5 years after the accident.

The release of thyroid antigen from radiation-damaged thyroid cells is the most likely mechanism triggering the autoimmune reaction after radiation injury, regardless of the modality of thyroid exposure.

5. Conclusion

The evidences accumulated in the last 15 years strongly indicate the strict dependency between post-Chernobyl radiation fallout and reported increase of thyroid tumors and autoimmune diseases.

Programs of long-term surveillance of the affected population and further molecular and immunological studies are needed to fully understand the more intimate mechanism through which ionizing radiation leads to thyroid cell damage.

Acknowledgements

This work has been supported in part by grants from: Associazione Italiana Ricerca sul Cancro (AIRC); European Union, INCO-COPERNICUS: project IC15-CT980314; and Ministero dell'Università della Ricerca Scientifica e Tecnologica (MURST) 1998.

References

[1] B.J. Duffy, P.J. Fitzgerald, Thyroid cancer in childhood and adolescents: a report on twenty-eight cases, Cancer 3 (1950) 1018–1032.
[2] A.B. Schneider, E. Shore-Freedman, R.A. Weistein, Radiation induced thyroid and other head and neck tumors: occurrence of multiple tumors and analysis of risk factors, J. Clin. Endocrinol. Metab. 63 (1986) 107–112.
[3] M.J. Favus, A.B. Schneider, M.E. Stachura, et al., Thyroid cancer occurring as a late consequence of head and neck irradiation. Evaluation of 1056 patients, N. Engl. J. Med. 294 (1976) 1019–1025.
[4] R.E. Shore, Issues and epidemiological evidence regarding radiation-induced thyroid cancer, Radiat. Res. 131 (1992) 98–111.
[5] S.L. Hancock, R.S. Cox, I.R. McDougall, Thyroid disease after treatment of Hodgkin's disease, N. Engl. J. Med. 325 (1991) 599–605.
[6] S. Nagataki, Y. Shibata, S. Inoue, N. Yokoyama, M. Izumi, K. Shimaoka, Thyroid disease among atomic bomb survivors in Nagasaki, J. Am. Med. Assoc. 272 (1994) 364–370.
[7] R.A. Conrad, D.E. Pegia, P.R. Larson, et al., Review of medical findings in a Marshallese population twenty-six years after accidental exposure to radioactive fallout, BNL 51261, MTIS, January1980, 1–138.
[8] F. Pacini, T. Vorontsova, E.P. Demidchik, et al., Post-Chernobyl thyroid carcinoma in Belarus children and adolescents: comparison with naturally occurring thyroid carcinoma in Italy and France, J. Clin. Endocrinol. Metab. 82 (1997) 3563–3569.
[9] H.R. Harach, E.D. Williams, Childhood thyroid cancer in England and Wales, Br. J. Cancer 72 (1995) 777–783.
[10] F. Pacini, T. Vorontsova, E. Molinaro, et al., Prevalence of thyroid autoantibodies in children and adolescents from Belarus exposed to the Chernobyl radioactive fallout, Lancet 352 (1998) 763–766.
[11] F. Vermiglio, M.G. Castagna, E. Volnova, et al., Post-Chernobyl increased prevalence of humoral thyroid autoimmunity in children and adolescents from a moderately iodine-deficient area in Russia, Thyroid 9 (1999) 781–786.
[12] K. Baverstock, B. Egloff, A. Pinchera, C. Ruchti, D. Williams, Thyroid cancer after Chernobyl, Nature 359 (1992) 21.
[13] E. Demidchik, V.S. Kazakov, L.N. Astakova, A.E. Okeanov, Y.E. Demidchik, Thyroid cancer in children after the Chernobyl accident: clinical and epidemiological evaluation of 251 cases in the Republic of Belarus, in: S. Nagataki (Ed.), Chernobyl: Update and Future. Proceedings of the Nagasaki Symposium, 1994, Elsevier, Amsterdam, 1994, pp. 21–30.

[14] B. Sobolev, I. Likhtarev, I. Kairo, N. Tronko, V. Oleynik, T. Bogdanova, Radiation risk assessment of the thyroid cancer in Ukrainian children exposed due to Chernobyl, in: A. Karaoglou, G. Desmet, G.N. Kelly, H.G. Menzel (Eds.), The Radiological Consequences of the Chernobyl Accident. Report No. EUR 16544 EN, Official Publications of the European Communities, Luxembourg, 1996, pp. 741–748.
[15] D. Williams, A. Pinchera, A. Karaoglou, K.H. Chadwich (Eds.), Thyroid Cancer in Children Living Near Chernobyl. Report No. EUR 15248 EN, Official Publications of the European Communities, Luxembourg, 1993, pp. 1–108.
[16] U.S. Kazakov, E.P. Demidchik, L.N. Astakova, Thyroid cancer after Chernobyl, Nature 359 (1992) 21.
[17] N. Tronko, T. Bogdanova, I. Kommissarenko, et al., Thyroid cancer in children and adolescents in Ukraine after the Chernobyl accident (1986–1995), in: A. Karaoglou, G. Desmet, G.N. Kelly, H.G. Menzel (Eds.), The Radiological Consequences of the Chernobyl Accident. Report No. EUR 16544 EN, Official Publications of the European Communities, Luxembourg, 1996, pp. 683–690.
[18] I.A. Liktarev, B.G. Sobolev, I.A. Kairo, et al., Thyroid cancer in the Ukraine, Nature 375 (1995) 365.
[19] A.F. Tsyb, E.M. Parshkov, V.V. Shaktarin, V.F. Stepanenko, V.F. Skvortsov, I.V. Chebotareva, in: A. Karaoglou, G. Desmet, G.N. Kelly, H.G. Menzel (Eds.), The Radiological Consequences of the Chernobyl Accident. Report No. EUR 16544 EN, Official Publications of the European Communities, Luxembourg, 1996, pp. 691–697.
[20] D.M. Parkin, C.S. Muir, S.L. Whelan, Y.T. Gao, J. Fenlay, J. Powell, Cancer Incidence in Five Continents, Int. Agency Res. Cancer Sci. Publ., vol. 120, International Agency for Research on Cancer, Lyon, 1992.
[21] L. Fugazzola, S. Pilotti, A. Pinchera, et al., Oncogenic rearrangements of the RET proto-oncogene in papillary thyroid carcinomas from children exposed to the Chernobyl nuclear accident, Cancer Res. 55 (1995) 5617–5620.
[22] S. Klugbauer, E. Lengfelder, E.P. Demidchik, H.M. Rabes, High prevalence of RET rearrangement in thyroid tumors of children from Belarus after the Chernobyl reactor accident, Oncogene 11 (1995) 2459–2467.
[23] M. Takahashi, J. Ritz, G.M. Cooper, Activation of a novel human transforming gene, ret, by DNA rearrangement, Cell 42 (1985) 581–588.
[24] Y.E. Nikiforov, J.M. Rowland, K.E. Bove, H. Monforte-Munoz, J.A. Fagin, Distinct pattern of ret oncogene rearrangements in morphological variants of radiation-induced and sporadic thyroid papillary carcinomas in children, Cancer Res. 57 (1997) 1690–1694.
[25] M. Santoro, F. Carlomagno, I.D. Hay, et al., Ret oncogene activation in human thyroid neoplasms is restricted to the papillary cancer subtype, J. Clin. Invest. 89 (1992) 1517–1522.
[26] I. Bongarzone, L. Fugazzola, P. Vigneri, et al., Age-related activation of the thyrosine kinase receptor proto-oncogenes RET and NTRK1 in papillary thyroid carcinoma, J. Clin. Endocrinol. Metab. 81 (1996) 2006–2009.
[27] Y. Nikiforov, D.R. Gnepp, Pediatric thyroid cancer after the Chernobyl disaster. Pathomorphologic study of 84 cases (1991–1992) from the Republic of Belarus, Cancer 74 (1994) 748–766.
[28] Y. Nikiforov, D.R. Gnepp, J.A. Fagin, Thyroid lesions in children and adolescents after the Chernobyl disaster: implications for the study of radiation tumorigenesis, J. Clin. Endocrinol. Metab. 81 (1996) 9–14.
[29] A.W. Furmanchuk, J.I. Averkin, B. Egloff, et al., Pathomorphological findings in thyroid cancers of children from the Republic of Belarus: a study of 86 cases occurring between 1986 ("post-Chernobyl") and 1991, Histopathology 21 (1992) 401–408.
[30] H.R. Maxon III, H.S. Smith, Radioiodine-131 in the diagnosis and treatment of metastatic well differentiated thyroid cancer, Endocrinol. Metab. Clin. North Am. 19 (1990) 685–718.
[31] A.M. Samuel, B. Rajashekharrao, Radioiodine therapy for well-differentiated thyroid cancer: a quantitative dosimetric evaluation for remnant thyroid ablation after surgery, J. Nucl. Med. 35 (1994) 1944–1950.
[32] V. Oliynyk, O. Epshtein, T. Sovenko, et al., Post-surgical ablation of thyroid residues with radioiodine in Ukrainian children and adolescents affected by post-Chernobyl differentiated thyroid cancer, J. Endocrinol. Invest. 24 (2001) 445–447.
[33] M. Ferdeghini, G. Boni, M. Grosso, et al., Outcome of post-Chernobyl papillary thyroid carcinomas treated by surgery, radioiodine and TSH-suppressive therapy, in: G. Thomas, A. Karaoglou, E.D. Williams (Eds.), Proceedings of an International Seminar on "Radiation and Thyroid Cancer", World Scientific, Singapore, 1999, pp. 481–486.

[34] L.J. De Groot, M. Reilly, K. Pinnamaneni, S. Refetoff, Retrospective and prospective study of radiation-induced thyroid disease, Am. J. Med. 74 (1983) 852.
[35] A.B. Schneider, E. Ron, J. Lubin, M. Stovall, T.C. Gierlowski, Dose–response relationship for radiation-induced thyroid cancer and thyroid nodules: evidence for prolonged effects of radiation on the thyroid, J. Clin. Endocrinol. Metab. 77 (1993) 362–369.

International Congress Series 1234 (2002) 185–192

Summary of the cytological diagnosis of childhood thyroid diseases around Chernobyl

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Abstract

A combination of ultrasonography and fine-needle aspiration biopsy was performed in the screening project on children around Chernobyl. The aspirated materials from 446 cases were analyzed cytologically. The ultrasonographical screening revealed a 2.9% prevalence of thyroid abnormalities. Fine-needle aspiration biopsy (FNA), conducted in 446 cases, revealed the following diseases: papillary carcinoma, 7.2%; follicular neoplasm, 10.3%; adenomatous goiter, 22.4%; chronic thyroiditis, 26.2%; and cyst, 22.9%. We evaluated the detail of findings of papillary carcinoma. Intranuclear inclusion and nuclear grooving were encountered in 75% and 85%, respectively. Psammoma body was encountered in about 50% of the cases. Nuclear atypism as defined by pleomorphism and the ratio of nucleus to cytoplasm were relatively conspicuous. The cytological characteristics of pediatric papillary carcinoma revealed diagnostic findings almost the same as those in adult cases, with the noteworthy exception of high prevalence of psammoma body, which seems to be specific to the Chernobyl cases. We also analyzed 47 cases of chronic thyroiditis diagnosed by fine-needle aspiration biopsy. Prominent epithelial hyperplasia was encountered in 23.4%, and Askinazy cell metaplasia was present in 55.3%. The presence of epithelial changes suggests that thyroiditis has existed for a long time or that thyroid follicles are destructed heavily in children. In this viewpoint, the Chernobyl cases are classified into auto-immune thyroiditis or Hashimato thyroiditis. This study suggests that childhood thyroid diseases, including both neoplasms and immunological disorders, are considered to be an ideal follow-up disease for monitoring the late effect of radioactive fallout.

Keywords: Thyroid cancer; Cytology; Childhood; Fine-needle aspiration biopsy

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PII: S0531-5131(01)00607-0

1. Introduction

An increase in thyroid cancer has been observed over the last 10 years among children in the Republic of Belarus, especially in regions in which severe iodine-radionuclide pollution occurred after the Chernobyl nuclear accident. Fine-needle aspiration biopsy (FNA) is known to be a useful strategy for the detection of thyroid papillary carcinoma. In fact, many pediatric cases have been identified by FNA in the screening study. Most pediatric thyroid cancers among the Chernobyl cases were papillary carcinoma, and they have different morphological features from adult cases in some particulars. There have been few available reports on cytological findings in pediatric papillary carcinoma around Chernobyl. To establish an accurate figure for the prevalence of thyroid cancer, meticulous screening and morphological confirmation of thyroid disorders are important. During visits to each center in the 1-year period, from June 1993 to March 1995, as a part of the Chernobyl Sasakawa Health and Medical Cooperation Project (CSHMCP), we performed FNA on children found to have thyroid abnormalities.

2. Subjects and methods

To investigate the prevalence of childhood thyroid diseases around Chernobyl, the screening by a combination of ultrasound examination and fine-needle aspiration biopsy (FNA) were performed in children in five oblasts in Belarus, Ukraine, and Russia. The centers involved in the CSHMCP are located in Mogilev (Belarus), Gomel (Belarus), western part of Bryansk (Russia), Kiev (Ukraine), and Zhitomir (Ukraine). These five centers (Mogilev, Gomel, Bryansk, Kiev, Zhitomir) cover areas with various degrees of radioactive contamination. The four oblasts were the administrative regions where radioactive contamination severely occurred, while the other oblast (Mogilev) served as control. Approximately 100,000 children, aged 0–10 years old at the time of the accident in 1986, were screened between May 1991 and March 1996. The screening revealed a 2.9% overall prevalence of ultrasonographical thyroid abnormalities. The prevalence of thyroid abnormalities was 1.39%, 6.30%, 3.31%, 2.67%, and 1.47% in Mogilev, Gomel, Bryansk, Kiev, and Zhitomir, respectively.

Ultrasonographical abnormalities over 5 mm in diameter, such as nodular lesions, cystic lesions, and abnormal echogenity, were chosen as targets for FNA. FNA was carried out with an echoguided syringe pistol (Chiba University Type) made to fit a 20-ml plastic syringe with a 22-gauge needle. Subjects were re-evaluated by Aloka 630 ultrasonography using a real time scanner with a 7.5-MHz probe. Four hundred forty-six subjects (154 nodules, 159 cysts, and 133 abnormal echogenities) received FNA according to the same biopsy criteria in the five centers. The aspirate was smeared on a microscopy slide, and then stained by May–Grunwald–Giemsa (MGG) staining.

3. Diagnostic criteria

The diagnostic criteria for each disorder were as follows. Papillary carcinoma featured intranuclear cytoplasmic inclusions, nuclear grooves, and irregular nuclear outlines in a cellular cluster, while follicular neoplasm featured many equal-sized microfollicular nests or rosette-like clusters. Chronic thyroiditis was diagnosed when many small lymphocytes and scattered plasma cells were encountered. Adenomatous goiter was diagnosed when follicular cells in sheets and clumps of various sizes, foamy cells, degenerative erythrocytes, and colloid were observed. The multiplicity of nodular and cystic lesions was taken into consideration for diagnosis of adenomatous goiter by ultrasonography. Cyst featured macrophages and colloidaspirate without epithelial cell clusters. Smears showing only bared nuclei or normal follicle cells without a proliferative nature were unclassified. The main lesion was registered for cytological diagnosis in this study when more than two lesions coexisted in a single case.

4. The prevalence of thyroid disease in abnormal ultrasonography

Papillary carcinoma was encountered in 32 children (7.2%) from only the contaminated oblasts. The prevalence of other thyroid diseases was: follicular neoplasm, 10.3%; adenomatous goiter, 22.4%; chronic thyroiditis, 26.2%; and cyst, 22.9%, suggesting that a major cause of thyroid abnormality is non-neoplastic changes, mainly chronic thyroiditis and cysts (Table 1). Chronic thyroiditis was most frequently observed in the contaminated oblast of Gomel and least frequently in the control oblast. These findings suggest that the childhood thyroid diseases, including both neoplasms and immunological disorders, increase in radiation-contaminated areas around Chernobyl. The highest incidence was found in Gomel, as was the highest cancer incidence, while the incidence of chronic thyroiditis was lowest in Mogilev. In the children with chronic thyroiditis, 84 out of 99 (84.9%) were positive for anti-thyroglobulin antibody (ATG) and/or anti-micosome antibody (AMC). Of the 109 children who were positive for ATG or AMC, 82 (75.2%) were diagnosed with chronic thyroiditis by FNA.

5. Ultasound sonography and cytology

The relation of ultrasonographical patterns to cytological diagnosis was shown in Table 2. Most cases of the papillary carcinoma were found in subjects showing a nodule pattern

Table 1
Results of fine-needle aspiration biopsy diagnosis

Country	City	Number of subjects	Cytological diagnosis						
			Papillary carcinoma	Medullary carcinoma	Follicular neoplasm	Adenomatous goiter	Cyst	Chronic thyroiditis	Unclassified
Belarus	Mogilev	32	1	0	1	7	11	7	5
	Gomel	111	22	0	14	20	27	24	4
Russia	Klincy	102	4	2	7	39	25	20	5
Ukraine	Kiev	30	1	0	1	4	8	7	9
	Korosten	171	4	0	23	30	31	59	24
Total		446	32	2	46	100	102	117	47
(%)		(100)	(7.2)	(0.4)	(10.3)	(22.4)	(22.9)	(26.2)	(10.5)

Table 2
Classification of the 446 subjects by ultrasonographic and fine-needle aspiration biopsy findings

Fine-needle aspiration biopsy findings	Ultrasonographic findings			Total
	Nodule	Cyst	Abnormal echogenity	
Papillary carcinoma	30	1	1	32
Medullary carcinoma	1	0	1	2
Follicular neoplasm	44	2	0	46
Adenomatous goiter	46	50	4	100
Cyst	16	80	6	102
Chronic thyroiditis	10	7	100	117
Unclassified	7	19	21	47
Total	154	159	133	446

by ultrasonography, while two cases were detected in cases showing cyst and abnormal echogenity. Chronic thyroiditis was detected mainly in subjects showing abnormal echogenity.

6. Characteristics of papillary carcinoma

In this study, we evaluated the cytological findings for papillary carcinoma in 32 cases, all for which tumor tissues that were amply sampled by FNA were available. The patients were 26 girls and 6 boys with ages ranging from 9 to 17 years, with a mean age of 12 years at operation. Their ages at the time of the accident ranged from 0.8 to 9.3 years, with a mean of 4.1 years. The growth pattern and cellular features were reviewed in each case, and the frequency, such as intranuclear cytoplasmic inclusion, nuclear grooving, multinucleated cell, psammoma bodies, stroma core, and oxyphilic change, was evaluated for each element. The degrees of nuclear atypism were classified into three grades as follows: Grade I, mild; Grade II, moderate; and Grade III, severe. Grade I is defined as cells showing uniform-sized nuclei and cytoplasm, and Grade III as cells having strong nuclear pleomorphism with high ratio of nucleus to cytoplasm (N/C ratio). These features are less pronounced than the nuclear atypism seen in undifferentiated carcinoma. Grade II included nuclear atypism intermediate between those in Grades I and III.

Table 3
Cytological features of papillary carcinoma diagnosed in 32 children

Findings	Number of cases	Proportion (%)
Intranuclear inclusion	25	78
Nuclear grooving	29	91
Papillary cluster	26	81
Monolayered sheet	26	81
Follicular structure	11	34
Psammomtous body	15	47
Hyalinized stroma	12	38
Multinucleated giant cells	13	41
Oxyphilic change	8	25

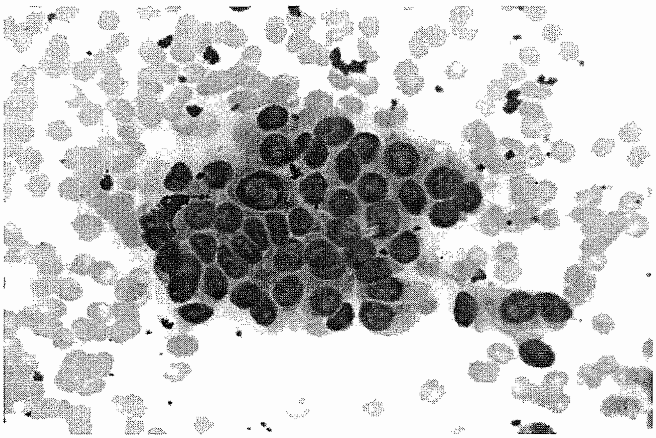

Fig. 1. Intranuclear pseudoinclusion and nuclear groove were present in a papillary cell cluster. This cell cluster was classified as Grade II.

The details of FNA findings are summarized in Table 3. Most cases had growth pattern characterized by monolayered cellular sheet. Papillary cell cluster was present in 81% of the cases. Colocalized follicular structure was present in 34% of the cases. This figure probably reflects the contribution of the solid-follicular subtype, which are prevalent patterns around Chernobyl. Intranuclear inclusion and nuclear grooving (Fig. 1) were encountered in 78% and 91%, respectively, and mutlinucleated giant cell was observed in 41%. Psammoma body was encountered in half of the cases, and in many of them, a few clustering foci of psammoma bodies were seen (Fig. 2). Stromal core was present in the center of papillary cell cluster in 38% of the cases. Oxyphilic change was a less-frequent finding. Nuclear atypism, as defined by pleomorphism and the N/C ratio, were relatively conspicuous, and most cases showed mixed nuclear atypism. Then, the results were subclassified into mixed nuclear atypism, e.g., Grade I+II and so on. No cases showed

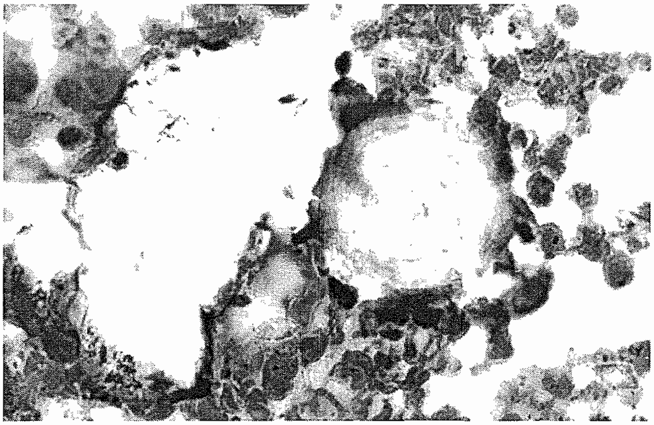

Fig. 2. Psammomatous bodies were recognized as a lamellar structure with a glassy, refractile appearance.

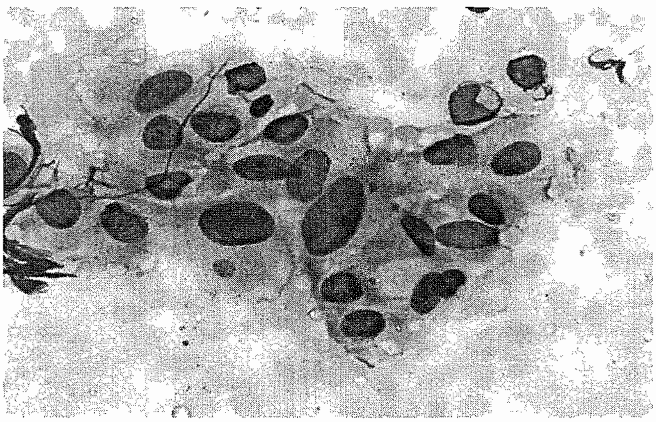

Fig. 3. Askanazy cells in chronic thyroiditis. Nuclear pleomorphism was occasionally associated.

simply Grade I. There were 15 cases (47%) with mild and moderate nuclear atypism (Grades I+II or II) and 17 cases (53%) with prominent nuclear atypism (Grades II+III or III).

7. Characteristics of chronic thyroiditis

We analyzed 47 cases of chronic thyroiditis diagnosed by FNA. All cases showed lymphocytic proliferation in variable degrees. Prominent epithelial hyperplasia was encountered in 11 cases (23.4%). Askinazy cell metaplasia (Fig. 3) was present in 26 cases (55.3%) in single-cell form and small-cell clusters. Pleomorphic nuclear changes were occasionally associated in Askinazy metaplasia. Of the 47 subjects with chronic thyroiditis, 7 were boys and 40 were girls, and the age ranged from 9 to 18 years (mean 13.9). Median values for TSH, free T4, ATG, and AMC in these subjects were 1.59 mIU/ml, 15.1 pmol/l, ×5, and ×360, respectively. The prevalence of AMC positivity in these chronic thyroiditis patients was slightly higher than that of ATG.

8. Discussion

The cytological diagnostic significance of the various features of the pediatric papillary carcinoma around Chernobyl was almost the same as that reported in the adult cases. Intranuclear cytoplasmic inclusion was a most useful finding and specific for papillary carcinoma, but 25% of the cases did not show intranuclear pseudoinclusions in this study. In such cases, the abundance of papillary cellular clusters and nuclear changes, including grooving and fine chromatin, were helpful findings. It is generally accepted that nuclear grooves are a useful criterion in the diagnosis of papillary thyroid carcinoma [1]. In our study, however, nuclear grooving was demonstrated in 85% of the cases, and this nuclear change is generally inconspicuous in MGG staining compared with Papanicolaou and hematoxylin and eosin staining as indicated by Francis et al. [2]. In contrast to this, the intranuclear cytoplasmic inclusion was more prominent than the nuclear grooving upon MGG staining. Papanicolaou staining is known as a useful staining method to evaluate the details of the nuclear character, but it has not been used routinely in Belarus because of constraints. In general, psammoma body is specific for papillary carcinoma, but the detection rate of this structure by FNA is not high, being generally around a fifth to a quarter of the cases [2]. In our study, psammoma body was observed in about half of the cases by FNA, and this might reflect the histological characteristics of pediatric papillary carcinoma in this area, especially considering that psammoma bodies were histologically present in all cases [3]. This fact supports the idea that physicians should pay attention to calcification in the nodular lesion by ultrasonography. It is reported that many of the childhood cancers in Belarus show aggressive features such as rapid growth, local invasion, and local metastasis [4]. Histologically solid components, recognized as poorly differentiated, are frequently present in Gomel cases [3]. The relatively high grade of nuclear atypism might reflect the poorly differentiated nature of the tumor.

Chronic thyroiditis was the most common cause of nontoxic goiters in childhood, accounting for 30% to 40% of these goiters [5]. In the present study, chronic thyroiditis was found in 31.0% of the children showing thyroid abnormality, this value being similar to that in the other studies. A significantly high incidence of chronic thyroiditis among atomic-bomb survivors exposed to low doses of radiation in Nagasaki was also reported [6]. In general, two basic patterns of thyroiditis are recognized in correspondence with the different phases of the disease. In older patients, the classical Hashimoto thyroiditis generally occurs, and the epithelial hyperplastic changes are encountered occasionally. In younger patients, the florid lymphocytic thyroiditis is common. The florid thyroiditis shows lymphocytic infiltration without epithelial changes, including hyperplasia and Askinazy metaplasia. However, in children around Cheronbyl, the epithelial hyperplasia and Askanazy metaplasia are the common features. The presence of epithelial changes suggests that thyroiditis has existed for a long time or that thyroid follicles are destructed heavily in children around Cheronbyl. In this viewpoint, thyroiditis around Chernobyl is classified to be autoimmune thyroiditis and Hashimato thyroiditis.

Our results provide the epidemiological evidence of cytologically diagnosed childhood thyroid diseases among children and suggest a high incidence of thyroid cancer and possibly also of autoimmune thyroid disease around Chernobyl [7]. In radiosensitive children, the thyroid may be affected, directly or indirectly, by either immediate exposure to radiation or continuous exposure to low-dose radiation in the contaminated area. This study suggests that childhood thyroid diseases, including both neoplasms and immunological disorders, are considered to be an ideal follow-up disease for monitoring the late effect of radioactive fallout.

Acknowledgements

The authors thank Noboru Takamura, Kiyoto Ashizawa, Hiroyuki Namba, Yoshisada Shibata (Atomic Bomb Disease Institute, Nagasaki University) and Garina Panasyuk (Gomel Specialized Medical Dispensary) for their cooperation.

References

[1] S. Bhambhani, V. Kashyap, D.K. Das, Nuclear grooves. Valuable diagnostic feature in May–Grunwald–Giemsa-stained fine-needle aspirates of papillary carcinoma of the thyroid, Acta Cytol. 36 (1990) 809–812.

[2] I.M. Francis, D.K. Das, Z.A. Sheikh, P.N. Sharma, S.K. Gupta, Role of nuclear grooves in the diagnosis of papillary thyroid carcinoma. A quantitative assessment on fine-needle aspiration smears, Acta Cytol. 39 (1994) 409–415.

[3] M. Ito, S. Yamashita, K. Ashizawa, T. Hara, H. Namba, M. Hoshi, Y. Shibata, I. Sekine, L. Kotova, G. Panasyuk, E. Demidchk, S. Nagataki, Histopathological characteristics of childhood thyroid cancer in Gomel, Belarus, Int. J. Cancer 65 (1996) 29–33.

[4] Y.E. Nikiforov, D.R. Gnepp, Pathomorphology of thyroid gland lesions associated with radiation exposure: the Chernobyl experience and review of the literature, Adv. Anat. Pathol. 6 (2) (1999) 78–91.

[5] M.L. Rallison, B.M. Dobyns, F.R. Keating, J.E. Rall, F.H. Tyler, Thyroid nodularity in children, JAMA, J. Am. Med. Assoc. 233 (1975) 1069–1072.

[6] S. Nagataki, Y. Shibata, S. Inoue, N. Yokoyama, M. Izumi, K. Shimaoka, Thyroid diseases among atomic bomb survivors in Nagasaki, JAMA, J. Am. Med. Assoc. 272 (1994) 364–370.

[7] M. Ito, S. Yamashita, K. Ashizawa, H. Namba, M. Hoshi, Y. Shibata, I. Sekine, S. Nagataki, I. Shigematsu, Childhood thyroid diseases around Chernobyl evaluated by ultrasound examination and fine-needle aspiration cytology, Thyroid 5 (1995) 365–368.

International Congress Series 1234 (2002) 193–200

Gene rearrangements in thyroid carcinomas after irradiation during childhood: lessons from the Chernobyl reactor accident

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Abstract

Papillary thyroid carcinomas (PTC) developed with a high incidence in children and young adults who had been exposed to radioactive fallout in contaminated regions of Belarus after the Chernobyl reactor accident. They are informative for a molecular genetic analysis of radiation-induced PTC. In contrast to spontaneous PTC, a high prevalence of gene aberrations was found with rearrangements of the receptor tyrosine kinase gene *RET* in the majority of cases and a few *NTRK1* rearrangements. In the rearranged form of *RET*, the transmembrane and extracellular parts are replaced by regulatory units of other genes. Among the fused genes, *ELE1* (*ARA70*) is most prevalent in PTC at short latency periods after irradiation, *H4* gene fusions prevail in later-occurring PTC. Both types of rearrangement, PTC3 and PTC1, respectively, are formed by intrachromosomal inversions on chromosome 10. Analysing *ELE1/RET* chimeric genes, we found radiation-induced DNA breakpoints localized exactly at or in close vicinity to topoisomerase I binding sites indicating a role for this enzyme in the formation of DNA breaks after irradiation. Breakpoints are distributed in the affected introns of both genes without significant clustering. They do not contain larger deletions of insertions. Short regions of sequence homology and short direct or inverted repeats were observed at the breakpoints suggesting microhomology-mediated DNA end joining as a mechanism in the fusion process. In addition to PTC1 and PTC3, we and others described several rare novel types of *RET* rearrangement, all formed by interchromosomal translocations, with parts of *RIα*, *GOLGA5*, *HTIF*, *RFG7*, *RFG8*, *KTN1*, and *ELKS* fused at the 5' end of the *RET* tyrosine kinase domain. These gene fusions appear to have in common an uncoupling of the *RET* tyrosine kinase from its physiological control due to an inherent dimerization potential. This may lead to constitutive, ligand-independent activation of *RET* tyrosine kinase in thyrocytes lacking this activity under normal conditions, and subsequent clonal expansion of the affected cells. It is evident from

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PII: S0531-5131(01)00608-2

our comparative study on a large number of PTC with *ELE1/RET* and *H4/RET* rearrangements after irradiation that the type of the *RET*-fused gene determines the tumor phenotype and may be decisive also for the clinical course of radiation-induced PTC.

Keywords: Papillary thyroid carcinoma; Gene rearrangement; DNA breakpoints; Irradiation; *RET*

1. Introduction

Epidemiological studies revealed a high transformation sensitivity of the thyroid gland after external irradiation, particularly during childhood [1]. A new dimension for analysing the underlying principles was opened by follow-up studies in radiation-exposed children and young adults after the Chernobyl reactor accident when huge amounts of radioactive isotopes, among others also high quantities of iodine radioisotopes [2], were released during a limited period of time. They led to contamination of inhabitants of parts of adjacent countries, most severely in southern Belarus. After a latent period of about 4 years, the first thyroid carcinomas [3,4] were observed in children in the heavily radioiodine-contaminated areas. Children exposed at an age of up to about 4 years at the time of exposure showed the highest incidence [5] of papillary thyroid carcinomas (PTC) [6,7]. In an attempt to disclose mechanisms of radiation-induced thyroid carcinogenesis, a large number of post-Chernobyl PTC (n=191) that were surgically removed between April 1993 and January 1998 were systematically analysed in our laboratory [8,9]. In contrast to findings in sporadic thyroid carcinomas, a majority of these tumors exhibited structural genetic aberrations, mainly gene rearrangements. DNA breakpoint analyses in a selected series of these tumors with a typical type of rearrangement (PTC3) will be summarized and will shed light on the mechanism of radiation-induced gene rearrangements. Our original work where details are described has been published [8–18].

2. The cohort of children and young adults

A total of 191 PTC was investigated that developed in 69 male and 122 female patients who had been exposed to radioactive fallout after the Chernobyl reactor accident at an age between 0 and 18 years. They formed an unselected representative cohort of tumors that developed 7–12 years after the Chernobyl reactor accident, mainly in Belarus [9]. The largest number of PTC was collected in the most highly contaminated parts of Belarus, the oblast Gomel (46.6%). Of all patients, 56.5% were at an age of 4 years or less at the time of exposure, 51.8% were <14 years at the time of surgery. Eighty-five percent had lymph node metastases. Histological classification according to the predominant structures revealed 30.9% typical papillary, 37.2% follicular, 22.0% solid and 3.1% diffuse sclerosing variants of PTC, besides mixed variants (6.3%). Deep-frozen tissues of the tumors were analysed for genetic aberrations.

3. Gene rearrangements

A high prevalence of rearrangements of the *RET* proto-oncogene was detected in post-Chernobyl PTC. Under normal conditions, *RET* is expressed in neural crest-derived cells, but not in thyrocytes. *RET* codes for a receptor tyrosine kinase. It is activated in a heterotrimeric complex with its ligand GDNF and GDNFRα [19]. Rearrangement leads to oncogenic activation: The 3′ end of *RET* that comprises the tyrosine kinase domain is fused to parts of other genes that permit ligand-independent activation of *RET*. Among the *RET*-fused genes, three types have been described before the Chernobyl reactor accident: PTC1, with a fusion of the *H4* gene of unknown function [20,21]; PTC2, where *RET* is fused to the regulatory subunit of the cAMP-dependent protein kinase A [22]; PTC3, with the fusion gene *ELE1* (*ARA70*) [23–25]. In post-Chernobyl tumors of the first decade after the accident (n=61), *RET* rearrangements were found in about two thirds of all PTC. Among them, PTC1 was detected in 23.7%, PTC3 in 63.2% of *RET* rearrangement-positive tumors. PTC2 was missing. In tumors with a latency period of more than 10 years after the reactor accident, the fraction of *RET* rearrangement-positive cases declined to 43.1% (Table 1). While in the early period a predominance of PTC3 rearrangements was observed, the later period was characterized by a switch from PTC3 to PTC1 rearrangements that comprised more than two thirds of all rearrangement-positive tumors (Table 2).

In addition to PTC1 and PTC3, various other types of *RET* rearrangements have been detected recently in post-Chernobyl PTC. In PTC5, a fusion of the carboxy terminal of *RET* with *GOLGA5* was found, coding for a Golgi integral membrane protein [26]. PTC6 is characterized by fusion of *RET* to the transcriptional coactivator *HTIF1* [13]. In PTC7, an *HTIF1* homolog is fused to *RET* at the 5′ end of the tyrosine kinase domain [13]. PTC8 contains a rearrangement of *RET* with a gene of yet unknown function [16] (Table 3). In other rare cases, a part of *ELKS*, a gene of unknown function, is fused to *RET* [27]. Very recently, an additional *RET* rearrangement has been described in PTC from Belarus with a fusion to kinectin [28].

The pattern of the newly formed chimeric genes follows the same basic principle: At the 3′ end, the tyrosine kinase domain is always preserved. The length to the upstream end of *RET* differs. In most cases, exon 11 is lost. Rarely a part of it remains preserved with an intraexonic breakpoint present (PTC4) [29]. However, in all cases, the 5′ end of *RET* that warrants the stringent control of *RET* activation, is replaced by the fused gene. It is characteristic to the fused genes that they are ubiquitously expressed, contain coiled-coil domains with dimerization potential and might thus lead to dimerization of the fusion protein. The hypothesis is proposed that dimerization induces a *RET* ligand-independent,

Table 1
Prevalence of *RET* rearrangements in PTC detected at different time intervals after the Chernobyl reactor accident

Tumor latency	*RET* rearrangement	Number of cases	Proportion
7–10 years	Present	38	62.3%
	Not detected	23	37.7%
> 10 years	Present	56	43.1%
	Not detected	74	56.9%

Table 2
Prevalence of various types of *RET* rearrangements in PTC during the early (≤10 years) (n=38) and later (>10 years) (n=56) periods after the Chernobyl reactor accident

Type of *RET* rearrangement	*RET*-fused gene	Latent period			
		First decade		>10 years	
		n	Proportion	n	Proportion
PTC1	*H4*	9	23.7%	39	69.9%
PTC2	*RIα*	0	0	0	0
PTC3	*ELE1* (*ARA70*)	24	63.2%	14	25.0%
PTC5	*GOLGA5*	1	2.6%	1	1.8%
PTC6	*HTIF*	1	2.6%	1	1.8%
PTC7	*HTIF* homolog	1	2.6%	0	0
PTC8	*RFG8*	2	5.3%	1	1.8%

constitutive activation of the *RET* tyrosine kinase and autophosphorylation, a prerequisite to triggering the signal transduction cascade that under normal conditions seems inactive in thyrocytes. This cell type-specific *RET* activation by release from normal control appears to be the critical step for malignant transformation of irradiated thyrocytes. However, biology of the developing thyroid carcinoma appears dependent also on the type of the *RET*-fused gene. As summarized in Table 3, at least some *RET*-fused genes belong to transcription coactivators with important functions in regulating transcription. Changes of these functions because of (partial) loss of these genes by rearrangements with *RET* may bear implications for the specific tumor phenotype. A study on relations between type of *RET* rearrangement and tumor phenotype revealed a highly significant prevalence of solid variants of PTC in PTC3, where *ELE1* is fused to *RET*, in contrast to papillary or follicular

Table 3
Types, function and chromosomal location of *RET*-fused genes (wild-type *RET* on chromosome 10q11.2)

Type of *RET* rearrangement	*RET*-fused gene	Function	Chromosomal location of *RET*-fused gene	Reference
PTC1	*H4*	Unknown	10q21	[20,21]
PTC2	*RIα*	Catalytic domain of cAMP-dependent kinase A	17q23	[22]
PTC3	*ELE1* (*ARA70*)	Transcription coactivator of androgen receptor	10q11.2	[23–25]
PTC5	*GOLGA5*	Golgi integral membrane protein	14q	[26]
PTC6	*HTIF1*	Transcription coactivator of nuclear receptors	7q32	[13,28]
PTC7	*RFG7*	*HTIF* homolog	1p13	[13,28]
PTC8	*RFG8*	Unknown	18q21-22	[16]
	ELKS	Unknown	12p13	[27]
	KTN1	Influence on microtubular organelle movement	14q22.1	[28]

variants of PTC in tumors bearing preferentially the PTC1 type of rearrangement (*H4/RET*). Further, the significantly higher prevalence of PTC3 in tumors with the shortest latency period after irradiation indicates a more rapid development as compared to PTC1, with higher prevalence at later intervals after the reactor accident. This assumption is corroborated by a significant correlation between the more advanced *pT3/T4* category and the presence of *ELE1/RET* rearrangements compared with the *H4/RET* type of rearrangement [9]. This observation may be relevant for the clinical prognosis.

Typically, *RET* rearrangements of highest prevalence (PTC1 and PTC3) are formed by intrachromosomal inversions on chromosome 10 where *RET* is located at 10q11.2. In contrast, interchromosomal translocations predominate in rare types of *RET* rearrangements (Table 3). Obviously, a specific mechanism is involved in breakpoint formation and recombination processes after DNA damage by irradiation favouring recombination by intrachromosomal inversion. To contribute to a better understanding of the mechanisms involved, we performed a genomic breakpoint analysis in 26 post-Chernobyl tumors with an *ELE1/RET* rearrangement. Except for very few intraexonic breakpoints in *RET* exon 11, all other *RET* breakpoints were found in *RET* intron 11. In contrast to former assumptions, there was no significant microclustering of the breakpoints in this part of *RET*. A similar breakpoint pattern without any significant clusters was found also in the *ELE1* gene. The area covered by breakpoints in this gene comprised about 2.3 kbp, including a small intron (522 bp), the following exon (144 bp) and the subsequent intron (1670 bp). Though two alu elements are present in this large intron, breakpoints or the corresponding fusion points do not show any clustering at these positions. Remarkably, only minor deletions and insertions were present in the *ELE1* or *RET* gene at the fusion points. However, almost all breakpoints were found in close vicinity to patches of microhomology in the wild-type sequences. These findings indicate that rearrangements were not the result of homologous recombination that would require larger stretches of homology. Instead, the results suggest that fusions are formed by nonhomologous DNA end-joining mechanisms. Details of these investigations are given elsewhere [18].

Usually it is assumed that double strand breaks are a prerequisite to gene rearrangements [30]. Double strand breaks in *ELE1* and *RET* genes might be the consequence of incorporation of high amounts of radioiodine into the thyroid gland. However, we found in our genomic analysis a significant abundance of strong and intermediate topoisomerase I binding sites at or near the fusion points of the two participating genes *ELE1* and *RET*. Topoisomerase I changes the superhelical state of DNA under a variety of conditions, including replication and recombination. It could be envisaged that the normal function of this enzyme, to induce a single strand break after formation of a covalent bond between DNA at the recognition sequence and the enzyme, could also lead to a double strand break when the enzyme is cross-linked by irradiation during DNA replication (for details see Ref. [18]). It is not yet clear whether such processes are involved in the generation of *ELE1/RET* rearrangements because adequate test systems are still missing.

The high prevalence of rearrangements formed by intrachromosomal inversions between genes located at close vicinity to each other on chromosome 10 (*ELE1* and *RET*, both at 10q11.2) suggests that the physical vicinity of the two genes is essential for this type of rearrangement. We speculated about the possibility that *ELE1* and *RET* could be located, at least temporarily, at the same chromatin loop which could bring the two genes close to each other and under the influence of the recombination machinery triggered into action by a single strand break. This and other possible models of rearrangements have been described [18].

4. Conclusions

Gene rearrangements appear to be typical, if not characteristic for radiation-induced PTC. Other genetic aberrations as found in various types of sporadic thyroid tumors do not play a major role in post-Chernobyl PTC. Exposure of the thyroid gland to high doses of radioiodine induces multiply DNA damage sites and may lead to single or double strand breaks without a preformed pattern in the genome. However, cells capable of repairing DNA damage are a population at risk for malignant transformation. In the thyroid gland, repair of DNA strand breaks occurring in a specific part of the *RET* proto-oncogene, in intron 11, or, in a few instances also in exon 11, represents a critical lesion for changing the regulation of the affected thyrocyte. The stringent control of *RET* tyrosine kinase activity by a complex interaction of the ligand-binding domain with ligand and a specific ligand-receptor molecule is suspended. Replacement of the extracellular part of *RET* by fusion with various kinds of ubiquitously expressed genes that have in common coiled-coil domains with putative potential for dimerization, triggers the preserved *RET* tyrosine kinase to ligand-independent constitutive activation. Despite many attempts in the past, consistent genetic alterations in addition to gene rearrangements have not yet been found in post-Chernobyl. The fact that different parts of the same primary tumor as well as lymph node metastases of the same patient exhibit identical *RET* rearrangements (unpublished observations) suggests that gene rearrangements of the *RET* type represent the most critical genetic change that putatively leads to clonal expansion and progression and may even be important for invasion and metastasis. The exact mechanisms of rearrangement are not yet known, but findings at gene fusion points suggest that chromosomal loops at the site where *ELE1* (or *H4*) and *RET* are located might play a role for bringing these genes most frequently involved into a position that allows microhomology-mediated recombination. Other mechanisms may be effective in the other rare *RET* rearrangements that involve interchromosomal translocations. They comprise less than 10% of all *RET* rearrangements found after Chernobyl. With the unifying concept at hand that *RET* rearrangements are important in radiation-induced thyroid carcinogenesis, it should not be overlooked that *RET*-fused genes seem to participate in the phenotype determination of the tumors, as became evident by comparing the biology and clinical behaviour of PTC1 and PTC3 tumors in our series of post-Chernobyl PTC large enough to draw a statistically valid conclusion. The underlying mechanisms are not well understood, mainly as not much is known about the exact physiological function of various *RET*-fused genes, and how the normal expression of these factors is influenced by balanced inter- or intra-chromosomal inversion.

Post-Chernobyl PTC will continue to serve as a most valuable tool to understand mechanisms of radiation-induced carcinogenesis and every effort should be made to use this unique chance.

Acknowledgements

Thanks are due to Professors E. Demidchik, D. Hoelzel, and E. Lengfelder, and to Drs. C. Beimfohr, A. Jauch, S. Klugbauer, P. Pfeiffer and S. Sidorow for expert cooperation in this project and for valuable discussion.

References

[1] E. Ron, J.H. Lubin, R.E. Shore, K. Mabuchi, B. Modan, L.M. Pottern, A.B. Schneider, M.A. Tucker, J.D. Boice, Thyroid cancer after exposure to external radiation: a pooled analysis of seven studies, Radiat. Res. 141 (1995) 259–277.

[2] S. Nagataki, K. Ashizawa, S. Yamashita, Cause of childhood thyroid cancer after the Chernobyl accident, Thyroid 8 (1998) 115–117.

[3] K. Baverstock, B. Egloff, A. Pinchera, C. Ruchti, D. Williams, Thyroid cancer after Chernobyl, Nature 359 (1992) 21–22.

[4] V.S. Kazakov, E.P. Demidchik, L.N. Astakhova, Thyroid cancer after Chernobyl, Nature 359 (1992) 21.

[5] F. Pacini, T. Vorontsova, E.P. Demidchik, E. Molinaro, L. Agate, C. Romei, E. Shavrova, E.D. Cherstvoy, Y. Ivashkevitch, E. Kuchinskaya, M. Schlumberger, G. Ronga, M. Filesi, A. Pinchera, Post-Chernobyl thyroid carcinoma in Belarus children and adolescents: comparison with naturally occurring thyroid carcinoma in Italy and France, J. Clin. Endocrinol. Metab. 82 (1997) 3563–3569.

[6] A.W. Furmanchuk, J.I. Averkin, B. Egloff, C. Ruchti, T. Abelin, W. Schäppi, E.A. Korotkevich, Pathomorphological findings in thyroid cancers of children from the Republic of Belarus: a study of 86 cases occurring between 1986 ('post-Chernobyl') and 1991, Histopathology 21 (1992) 401–408.

[7] Y.E. Nikiforov, D.R. Gnepp, Pediatric thyroid cancer after the Chernobyl disaster, Cancer 74 (1994) 748–766.

[8] H.M. Rabes, S. Klugbauer, Molecular genetics of childhood papillary thyroid carcinomas after irradiation: high prevalence of *RET* rearrangement, Rec. Res. Cancer Res. 154 (1998) 248–264.

[9] H.M. Rabes, E.P. Demidchik, J.D. Sidorow, E. Lengfelder, C. Beimfohr, D. Hoelzel, S. Klugbauer, Pattern of radiation-induced *RET* and *NTRK1* rearrangements in 191 post-Chernobyl papillary thyroid carcinomas: biological, phenotypic, and clinical implications, Clin. Cancer Res. 6 (2000) 1093–1103.

[10] C. Beimfohr, S. Klugbauer, E.P. Demidchik, E. Lengfelder, H.M. Rabes, *NTRK1* rearrangement in papillary thyroid carcinomas of children after the Chernobyl reactor accident, Int. J. Cancer 80 (1999) 842–847.

[11] S. Klugbauer, E. Lengfelder, E.P. Demidchik, H.M. Rabes, High prevalence of *RET* rearrangement in thyroid tumors of children from Belarus after the Chernobyl reactor accident, Oncogene 11 (1995) 2459–2467.

[12] S. Klugbauer, E.P. Demidchik, E. Lengfelder, H.M. Rabes, Detection of a novel type of *RET* rearrangement (PTC5) in thyroid carcinomas after Chernobyl and analysis of the involved *RET*-fused gene *RFG5*, Cancer Res. 58 (1998) 198–203.

[13] S. Klugbauer, H.M. Rabes, The transcription coactivator *HTIF1* and a related protein are fused to the *RET* receptor tyrosine kinase in childhood papillary thyroid carcinomas, Oncogene 18 (1999) 4388–4393.

[14] S. Klugbauer, E.P. Demidchik, E. Lengfelder, H.M. Rabes, Molecular analysis of new subtypes of *ELE/RET* rearrangements, their reciprocal transcripts and breakpoints in papillary thyroid carcinomas of children after Chernobyl, Oncogene 16 (1998) 671–675.

[15] H.M. Rabes, S. Klugbauer, Radiation-induced thyroid carcinomas in children: high prevalence of *RET* rearrangement, Verh. Dtsch. Pathol. Ges. 81 (1997) 139–144.

[16] S. Klugbauer, A. Jauch, E. Lengfelder, E. Demidchik, H.M. Rabes, A novel type of *RET* rearrangement (PTC8) in childhood papillary thyroid carcinomas and characterization of the involved gene (*RFG8*), Cancer Res. 60 (2000) 7028–7032.

[17] S. Klugbauer, E. Lengfelder, E.P. Demidchik, H.M. Rabes, A new form of *RET* rearrangement in thyroid carcinomas of children after the Chernobyl reactor pattern, Oncogene 13 (1996) 1099–1102.

[18] S. Klugbauer, P. Pfeiffer, H. Gassenhuber, C. Beimfohr, H.M. Rabes, *RET* rearrangements in radiation-

induced papillary thyroid carcinomas: high prevalence of topoisomerase I sites at breakpoints and microhomology-mediated end joining in *ELE1* and *RET* chimeric genes, Genomics 73 (2001) 149–160.
[19] M.A. Pierotti, P. Vigneri, I. Bongarzone, Rearrangements of *RET* and *NTRK1* tyrosine kinase receptors in papillary thyroid carcinomas, Rec. Res. Cancer Res. 154 (1998) 237–247.
[20] M.A. Pierotti, M. Santoro, R.B. Jenkins, G. Sozzi, I. Bongarzone, M. Grieco, N. Monzini, M. Miozzo, M.A. Herrmann, A. Fusco, I.D. Hay, G. Della Porta, G. Vecchio, Characterization of an inversion on the long arm of chromosome 10 juxtaposing *D10S170* and *RET* and creating the oncogenic sequence RET/PTC, Proc. Natl. Acad. Sci. U. S. A. 89 (1992) 1616–1620.
[21] M. Grieco, M. Santoro, M.T. Berlingieri, R.M. Melillo, R. Donghi, I. Bongarzone, M.A. Pierotti, G. Della Porta, A. Fusco, G. Vecchio, PTC is a novel rearranged form of the *ret* proto-oncogene and is frequently detected in vivo in human thyroid papillary carcinoma, Cell 60 (1990) 557–563.
[22] I. Bongarzone, N. Monzini, M.G. Borrello, C. Carcano, G. Ferraresi, E. Arighi, P. Mondellini, G. Della Porta, M.A. Pierotti, Molecular characterization of a thyroid tumor-specific transforming sequence formed by the fusion of *ret* tyrosine kinase and the regulatory subunit *RIα* of cyclic AMP-dependent protein kinase A, Mol. Cell Biol. 13 (1993) 358–366.
[23] I. Bongarzone, M.G. Butti, S. Coronelli, M.G. Borello, M. Santoro, P. Mondellini, S. Pilotti, A. Fusco, G. Della Porta, M.A. Pierotti, Frequent activation of *ret* proto oncogene by fusion with a new activating gene in papillary thyroid carcinomas, Cancer Res. 54 (1994) 2979–2985.
[24] M. Santoro, N.A. Dathan, M.T. Berlingieri, I. Bongarzone, C. Paulin, M. Grieco, M.A. Pierotti, G. Vecchio, A. Fusco, Molecular characterization of RET/PTC3; a novel rearranged version of the *RET* proto oncogene in a human thyroid papillary carcinoma, Oncogene 9 (1994) 509–516.
[25] F. Minoletti, M.G. Butti, S. Coronelli, M. Miozzo, G. Sozzi, S. Pilotti, A. Tunnacliffe, M.A. Pierotti, I. Bongarzone, The two genes generating RET/PTC3 are localized in chromosomal band 10q11.2, Genes, Chromosomes Cancer 11 (1994) 51–57.
[26] R.A. Bascom, S. Srinivasan, R.L. Nussbaum, Identification and characterization of golgin-84, a novel Golgi integral membrane protein with a cytoplasmic coiled-coil domain, J. Biol. Chem. 274 (1999) 2953–2962.
[27] T. Nakata, Y. Kitamura, K. Shimizu, S. Tanak, M. Fujimori, S. Yokoyama, K. Ito, M. Emi, Fusion of a novel gene, *ELKS*, to *RET* due to translocation t(10;12)(q11;13) in a papillary thyroid carcinoma, Genes, Chromosomes Cancer 25 (1999) 97–103.
[28] K. Salassidis, J. Bruch, H. Zitzelsberger, E. Lengfelder, A.M. Kellerer, M. Bauchinger, Translocation t(10;14)(q11.2;q22.1) fusing the kinectin to the *RET* gene creates a novel rearranged form (PTC8) of the *RET* proto-oncogene in radiation-induced childhood papillary thyroid carcinoma, Cancer Res. 60 (2000) 2786–2789.
[29] L. Fuggazola, M.A. Pierotti, E. Vigano, F. Pacini, T.V. Vorontsova, I. Bongarzone, Molecular and biochemical analysis of RET/PTC4, a novel oncogenic rearrangement between *RET* and *ELE1* genes, in a post-Chernobyl papillary thyroid cancer, Oncogene 13 (1996) 1093–1097.
[30] P.E. Bryant, The signal model: a possible explanation for the conversion of DNA double-strand breaks into chromatid breaks, Int. J. Radiat. Biol. 73 (1998) 243–251.

International Congress Series 1234 (2002) 201–204

Ten-year Chernobyl aid programmes of the Otto Hug Strahleninstitut-MHM: treatment and research projects on thyroid cancer in Belarus

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Abstract

The unexpected serious increase in the incidence of thyroid cancer following the reactor accident in Chernobyl led to considerable research efforts from abroad and the support of Belarus in order to mitigate these health problems. In 1991, the Otto Hug Strahleninstitut-MHM (Otto Hug Radiation Institute), a German non-governmental medical–scientific charity organization, started several long-term aid programmes and treatment and research projects on thyroid cancer and other diseases of this organ. Since 1993, the project "Thyroid Center Gomel" had more than 70 000 patients from this region for the diagnosis and treatment of thyroid diseases including cancer. The project of the "Pathological Anatomical Laboratory" is situated in the Oncological Dispensary in Minsk, where all childhood and juvenile and many adult thyroid cancers of Belarus are operated. More than 6500 thyroid tumours were diagnosed, preparing over 30 000 pathological slides. In 1997, the project of "Radioiodine Therapy" started in Gomel, giving treatment to more than 450 patients since that time. Since 1992, a fruitful international scientific cooperation on the pathology and molecular genetics of thyroid cancer resulted in a considerable progress in the understanding of this disease and in the installation of a tumour tissue bank.

Keywords: Chernobyl; Thyroid cancer; Thyroid pathology; Medical care; Tissue bank

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PII: S0531-5131(01)00609-4

1. Introduction

Among the CIS countries, the Republic of Belarus has received the biggest part of the radioactive release after the reactor accident in Chernobyl. Belarus does not have the capacity to face the enormous costs of remedying the Chernobyl effects on its own, and it is insufficient to report and investigate only the plight of the affected population. It is our moral obligation to support them as has also been emphasised by the Secretary General of the United Nations. In contrast to the predictions of the International Chernobyl Project in 1991 released by the advisory committee of IAEA, the affected regions of the three countries, in particular Belarus, experienced dramatic increases in the incidence of thyroid cancer in children. Additionally, in contrast to the statements of the UN-Committee UNSCEAR in 2000, the incidence of thyroid cancer in adults in the meantime also increased dramatically in Belarus by a factor of about 5.

2. The medical programmes of the Otto Hug Strahleninstitut-MHM in Belarus

After studying the health system and the available possibilities under the situation of the post-soviet time, it became clear that it would be preferable and more effective to install and equip suitable diagnosis and treatment facilities inside the country instead of taking selected patients for medical procedures abroad. Moreover, it appears that it is unacceptable to perform research programmes on the state of health and use the biological material of the patients if their complete medical treatment and after-care are not included or guaranteed.

Following these principles, the Otto Hug Strahleninstitut, a German non-governmental medical–scientific charity organization, started several long-term aid programmes and treatment and research projects on thyroid cancer and other diseases of this organ in 1991 (Table 1). At that time, the incidence of thyroid cancer in children in Belarus had already risen 30-fold over the mean incidence 10 years before the Chernobyl accident. According its statute, the Otto Hug Strahleninstitut, after the events or in situations with radiological exposure, gives the affected people humanitarian aid and health protection. The relief measures have to be accompanied by the qualified scientific investigation of the radiological situation and the examination of the health disorders in order to increase the knowledge of the processes of the development of radiation-induced diseases, and to get the information for the adaptation and improvement of the measures for the actual needs. It is a principle of all medical aid programmes of the Otto Hug Strahleninstitut that the medical care has the priority over scientific investigation since it is the standard in leading clinics worldwide.

Five out of these eight programmes are directly associated with the diagnosis, treatment and after-care of thyroid diseases including thyroid cancer in children, juveniles and adults and the further education and training of the staff. The programmes are also the basis of an international scientific collaboration with the scientists of the institutions in Belarus being supported and several research groups in the west.

Since 1993, the project "Thyroid Center Gomel" had more than 70 000 patients from this region for the diagnosis, internal treatment of thyroid diseases including cancer and

Table 1
List of the long-term programmes and projects of the Otto Hug Strahleninstitut-MHM in Belarus (year when the programme started and main institutions being supported)

(1) Radiometric Control of Food and Territories (1991) Centers of Hygiene and Epidemiology, Public Health Departments
(2) Prenatal Diagnostics–Genetic Consultation (1994) Oblast Center of Genetic Consultation, Gomel
(3) Equipping of Hospitals (1991) Hospitals and Dispensaries in Belarus
(4) Thyroid Center in Gomel (1992) Endocrinological Dispensary of Oblast Gomel
(5) Pathological Anatomical Laboratory (1992) Oncological Dispensary of the City of Minsk, Medical High School, National Thyroid Center of Belarus
(6) Radioiodine Treatment of Patients with Thyroid Tumours (1996) Oncological Dispensary of Oblast Gomel
(7) Further Education (Medicine, Medical Technology, Radioecology) (1991) Health services of all levels, University and Medical High School of Minsk, International Sakharov University of Radioecology, Minsk
(8) Thyroid Endocrinology Laboratory in Minsk (1997) Oncological Dispensary of the City of Minsk, Medical High School, National Thyroid Center of Belarus

medical after-care and performed more than 150 000 thyroid status blood tests using luminescence immune assays. The work of the hormone laboratory of this project is regularly tested for its quality through the participation in an international quality test programme.

The project of the "Pathologic Anatomical Laboratory," its routine work started in 1995, is in collaboration with the Belarussian National Thyroid Center and is situated in the clinic where all childhood and juvenile and many adult thyroid cancers of Belarus are operated. Until the spring of 2001, more than 6500 thyroid tumours were diagnosed, preparing over 30 000 pathological slides for the differential diagnosis of various types of thyroid tumours according to internationally accepted standards. During the last months of 1997, the new project of "Radioiodine Therapy" started in Gomel. This is of particular importance for Belarus because it includes also the long-term aftercare and controlled medication of the patients with L-thyroxine, taking advantage of the possibilities of the Gomel Thyroid Center. About 50% of the children with thyroid cancer in Belarus come from the region of Gomel. The value of the goods and services, which have been given to Belarus on the basis of the programmes of the Otto Hug Strahleninstitut for all projects until spring of 2001, is more than 22 million Deutsche mark.

3. Results of the scientific work under the Chernobyl aid programmes

The Chernobyl aid programmes of the Otto Hug Strahleninstitut were also the basis for many international research activities and collaborations, in particular not only on cancer and other disorders of the thyroid but also on other health disorders. This resulted in more than 30 scientific papers. Since 1992, a fruitful international cooperation on the pathology and molecular genetics of thyroid cancer resulted in a considerable progress in the understanding of the molecular processes involved in this disease. A few examples of the results of this scientific work are given in Refs. [1–5]. In the course of this long-term international cooperation, a tumour tissue bank has been set up, which in the meantime consists of a large number of samples. Further studies on the radiation-induced thyroid cancer depend on this tissue bank, which also help in getting more funding necessary for the medical therapy of the increasing number of thyroid cancer patients in Belarus after Chernobyl.

References

[1] S. Klugbauer, E. Lengfelder, E.P. Demidchik, H.M. Rabes, High prevalence of RET rearrangement in thyroid tumours of children from Belarus after the Chernobyl reactor accident, Oncogene 11 (1995) 2459–2467.

[2] E. Lengfelder, E. Demidschik, J. Demidschik, K. Becker, H.M. Rabes, L. Birukowa, 10 Jahre nach der Tschernobyl-Katastrophe: Schilddrüsenkrebs und andere Folgen für die Gesundheit in der GUS, Muench. Med. Wochenschr. 138 (15) (1996) 259–264.

[3] L. Lehmann, H. Zitzelsberger, A.M. Kellerer, H. Braselmann, U. Kulka, V. Georgiadou-Schuhmacher, T. Negele, F. Spelsberg, E. Demidchik, E. Lengfelder, M. Bauchinger, Chromosome translocations in thyroid tissues from Belorussian children exposed to radioiodine from Chernobyl accident measured by FISH-painting, Int. J. Radiat. Biol. 70 (5) (1996) 513–516.

[4] H.M. Rabes, E.P. Demidchik, J.D. Sidorov, E. Lengfelder, C. Beimfohr, D. Hoelzl, S. Klugbauer, Pattern of radiation-induced RET and NTRK1 rearrangements in 191 post-Chernobyl papillary thyroid carcinomas: biological, phenotypic and clinical implications, Clin. Cancer Res. 6 (2000) 1093–1103.

[5] E. Lengfelder, E. Demidtschik, J. Demidtschik, H.M. Rabes, J.D. Sidorow, P. Knesewitsch, Ch. Frenzel, 14 Jahre nach Tschernobyl: Schilddrüsenkrebs nimmt zu, Muench. Med. Wochenschr. 142 (16) (2000) 353–354.

International Congress Series 1234 (2002) 205–214

Results of radioactive iodine treatment in children from Belarus with advanced stages of thyroid cancer after the Chernobyl accident

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Abstract

Exposure of the thyroid to ionising radiation leads to an increased cancer risk. Whereas the average excess relative risk after external exposure amounts to approximately 8 per Gy, this relative risk is lower by a factor of 2 after exposure to radioiodine. The risk is greatest in newborns and small children below age of 5, intermediate in adolescents and questionable in adults. Papillary thyroid cancer with a relative incidence of approximately 80% per se is typical for thyroid cancer in childhood and adolescence; however, after exposure to radioiodine, this relative frequency is increased close to 100%. Bilateral involvement, multicentric growth and cancer not limited to the thyroid gland seem to be characteristic for radiation-induced thyroid cancer. Up to now, approximately 1500 cases of thyroid cancer in children below age of 15 have been diagnosed between 1990 and 2000 after the Chernobyl accident in Belarus, the Ukraine and Russia. Histologically, 94% of the tumors were classified as papillary thyroid cancer and tumors with stage pT1 in 26%, pT2 in 28%, pT3 in 1% and pT4 in 45%. Between 1st of April 1993 and 31st of December 2000, 209 children from Belarus with most advanced stages of thyroid cancer have been treated totally with 755 courses of radioiodine therapy in Germany. Of those selected cases, 71% were staged as pT4, 97% as pN1 and 46% as pM1. Disseminated miliary spread was typical for lung metastases detectable in 97 of those children. Up to now, complete remissions of tumor disease could be achieved in 84% of the whole group (and in 67% of the children with distant metastases). Fortunately, in no single case treated with radioiodine progressive disease or a recurrence has been observed up to now.

Keywords: Childhood thyroid cancer; Chernobyl; Radioiodine treatment

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PII: S0531-5131(01)00610-0

1. The Chernobyl accident

During the night from 25th to 26th of April 1986, the most severe reactor accident happened at the nuclear power plant Chernobyl 30 km south from the border of the Ukraine to Belarus. The reactor core exploded and caught fire, which could be extinguished not earlier than on the 9th of May 1986. Due to the burning graphite, enormous amounts of radioactivity were released during the first 10 days. According to recent calculations, approximately 12×10^{18} Bq ($\cong 0.3$ billion Ci) of radioactivity were released, among them 1.8×10^{18} Bq of I-131. The radioactivity was transported with the prevailing winds from the northern parts of the Ukraine to Belarus and the western parts of Russia, and later Scandinavia and parts of western Europe. Belarus has been most heavily contaminated with 70% of the released activity. Extremely high contaminations have been found in the regions surrounding the cities of Gomel and Brest [1].

2. Thyroid cancer in Belarus after Chernobyl

The frequency of thyroid cancer in children from Belarus, the Ukraine and the western parts of Russia is increasing since 1990 [2–6]. Totally, in the three republics afflicted by radioactive fallout from the Chernobyl accident, approximately 1500 cases of thyroid cancer in children below age of 15 have been diagnosed between 1990 and 1998, as compared to approximately 100 cases diagnosed between 1968 and 1989 [2–6].

The most reliable epidemiological data seem to be available from Belarus [2,3]. The relative incidence of thyroid cancer per 100 000 children below age of 15, which amounted to 0.1–0.3 between 1986 and 1989, increased to 4.0 in 1995 (Fig. 1). In the region of Gomel, which has been most heavily contaminated after the Chernobyl accident by radioactive fallout containing I-131 and short-lived radioisotopes of iodine, the relative incidence increased to 13.5 in 1995. Since 1996, the relative incidence of thyroid cancer in children is decreasing (Fig. 1).

Fig. 1 shows that the relative incidence of thyroid cancer in adults from Belarus as well is increasing since 1986. However, whereas the increase in children is approximately 20-fold comparing the year 1995 to the mean of the years 1986–1989, the increase of the relative incidence in adults between 1986 and 1997 is fivefold only. According to actual data of the Survival Epidemiology and End Results Programme [7] from the USA, the yearly incidence of thyroid cancer between 1990 and 1994 amounted to 4.9 per 100 000 inhabitants (women 6.9, men 2.8 per 100.000). In children and adolescents below age of 20, the incidence was 0.1 per 100 000 US inhabitants. Between 1950 and 1994, the incidence of thyroid cancer in the USA increased by approximately 22% [7]. This comparison shows that the incidence of thyroid cancer in children from Belarus, which was comparable to the incidence in the USA before 1990, increased without any doubt after the Chernobyl reactor accident. On the contrary, the incidence of thyroid cancer in adults from Belarus was lower by a factor of 2 in 1986 and at the end of the observation period in 1997, the incidence in Belarus was approximately twofold higher as compared to adults from the USA. This increase in adults may be related to the Chernobyl accident too, since children exposed in 1986 at the age of 4 and older changed in 1997 from the cohort of children and adolescents below age of

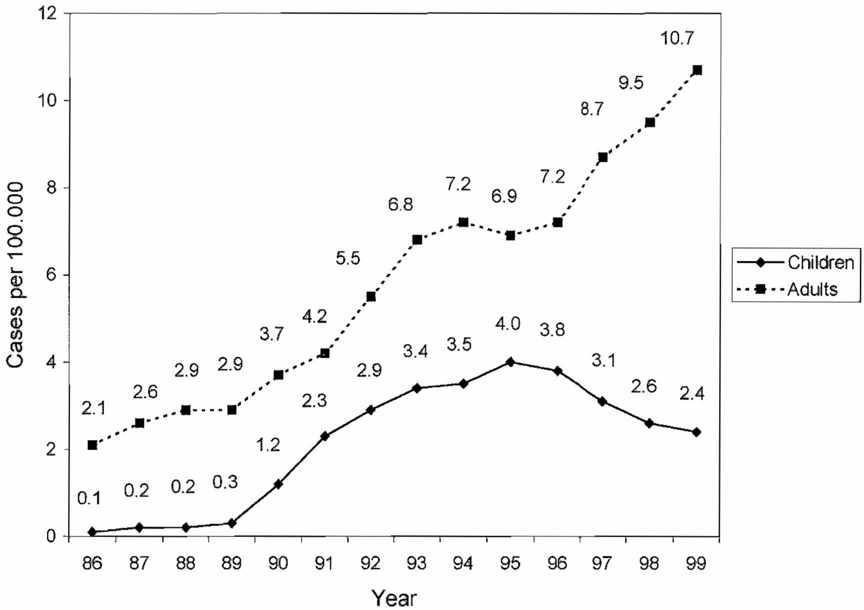

Fig. 1. Annual incidence of thyroid cancer from 1986 to 1999 in adults and children below the age of 15 years in Belarus.

15 years into the cohort of adults. On the other hand, it has to be considered that the incidence rate of 10.7 cases per 100 000 adults lies in between the world wide variability of incidence rates from 0.2 to 8.8 for men and 0.8 to 18.2 for women [8].

The mean dose to the thyroid of the 500 000 children from Belarus exposed to irradiation amounted to 0.4 Gy (25 percentile 0.08, 75 percentile 1.0 Gy) [9]. After correction for the dependence of average thyroid doses on age, the radiation-induced absolute thyroid risk in Gomel is about a factor of 3 higher for children up to the age of 10 years at exposure compared to older ones. Up to 10 years of age at exposure, the sex ratio females/males is about 1.5. After puberty, the ratio increases. Taking the data together, an excess absolute risk of 2.3 (95% CI 1.4–3.8) per 10^4 person-year Gy for children below age of 15 can be calculated [10]. This is a factor of 2 lower than the best estimate derived from the pooled study of thyroid cancer after external exposures [11]. Projecting the age-adjusted average excess risk per unit thyroid dose for the period of 5–50 years following the Chernobyl accident, it has been estimated that about 15 000 cases (95% CI 5000–45 000) may develop [12].

As a whole, 673 cases of childhood thyroid cancer have been detected and operated by the Centre for Thyroid Tumors in Minsk between 1986 and 1997 [2,3]. Of those children, 52% lived in the Gomel region. Histologically, 94% of the tumors were classified as papillary thyroid cancer. At the time of surgical intervention in Minsk, 26% of the cases had to be staged as pT1 (tumors of less than 1 cm of diameter), 28% as pT2 (between 1 and 4 cm of diameter), 1% as pT3 (more than 4 cm of diameter without invasion of surrounding tissue) and 45% as the most advanced stage pT4 (tumors invading soft tissue surrounding the thyroid gland). In 25% of tumors stage pT1–2 and 45% of tumors stage pT4, cancer growth was classified histologically as multicentric. In 50% of the cases stage pT1–3 and 81% of patients stage pT4, lymph node metastases have been observed during surgery. The relative frequency of distant metastases diagnosed in Minsk immediately postoperatively amounted to 5% in tumor stages pT1–3 and 24% in tumor stage pT4.

3. Treatment of thyroid cancer in children from Belarus

The German project "Scientists help Chernobyl Children" has been established in the framework of a bilateral cooperation between two centres in Minsk and the University Clinics for Nuclear Medicine in Essen and later Würzburg. Surgical resection of thyroid tumors and removal of lymph nodes have been performed by the surgical team of the Centre for Thyroid Tumors in Minsk. Radioiodine treatment and staging with nuclear medicine procedures was the task of the Clinics for Nuclear Medicine in Essen and Würzburg, respectively. Follow-up was performed in Minsk by the Centre for Thyroid Tumors and the Research and Clinical Institute of Radiation Medicine and Endocrinology in Minsk.

3.1. Patients

Between the 1st of April 1993 and the 31st of March 2000, 209 children from Belarus with most advanced stages of thyroid cancer have been selected for treatment in Germany (Table 1). A total of 755 courses of I-131 therapy have been applied until the 31st of March 2000.

Table 1
Children with thyroid cancer from Belarus treated with I-131 in Germany between 1st of April 1993 and 31st of December 2000

Patients	209 Children		
	755 Treatment courses		
Origin	91 Gomel area		
	118 Other parts of Belarus		
Gender	119 Girls		
	90 Boys		
Age	7–18 years (11.9±2.5)		
Histology	207 Papillary cancers		
	2 Follicular cancers		
Stage	pTx—2	pNo—6	pMo—112
	pT1—3	pN1—203	pM1—97
	pT2—51		95 Lung
	pT3—4		2 Bone
	pT4—149		1 Brain
Pretreatment	39 Radioiodine therapies in Minsk		
	5 Radioiodine therapies in Italy		
	19 Percutaneous irradiations		
	6 Chemotherapies		

Forty-four percent of the children originated from the heavily contaminated Gomel region. The mean age of the children at the time of the reactor accident was 2.6±2.2 years (78% of the children were below age of 5). Their mean age at the time of surgery ranged from 7 to 18 years with a mean age of 11.9±2.5 years. This corresponds to a mean latency time of approximately 9 years; the shortest time interval between exposure and surgery was 3.2 years. Of the total number of the children, 59% were female, 41% male; 99% of the cancers were typed histologically as papillary and 1% as follicular carcinomas.

Seventy-one percent of the cases selected for treatment in Germany because of the aggressiveness of tumors had to be classified as stage pT4. In 97% of the cases lymph node metastases and in 46% of the children distant metastases had been detected. With the exception of two cases with secondaries to bone, distant metastases were localized in the lungs (among those cases, one child with metastases to lungs and brain). Nearly all of the cases with lung metastases presented as disseminated miliary spread, only 4% of the children showed single localized nodular lesions. Only 53% of the children with lung metastases detectable by I-131 scanning showed positive thorax X-rays; this proportion was higher (82%) for high resolution computed tomography. In 44 of the 209 children, radioiodine treatment had been performed with different activities in Minsk (mainly low activities up to 1 GBq) and previously in Italy; 19 of the children had been irradiated percutaneously with mainly low radiation doses (up to 20 Gy). In six children, chemotherapy with different drugs had been performed in Minsk.

3.2. Protocol

The diagnostic protocol included ultrasonography and scintigraphy of the neck, thorax X-ray, computer tests of pulmonary function, determinations of thyroglobulin, TSH, free T_4 and free T_3 in serum as well as measurements of calcium, phosphate and differential blood cell counts. Additionally, X-ray computed tomography (CT), whole-body counter measurements of incorporated radionuclides and biological dosimetry have been performed in a subset of children.

For treatment, 50 MBq of I-131 per kg of bodyweight have been applied to eliminate thyroid remnants. For ablation of metastases, 100 MBq of I-131 per kg of bodyweight were given. Simultaneously, antiemetica and emulsions for the protection of gastric mucosa were given to reduce gastrointestinal side effects. Two days after treatment, replacement therapy with levothyroxine, which had been withdrawn 4 weeks before treatment, was restarted. The mean dose amounted to 2.5 μg of levothyroxine per kg of bodyweight. For staging, whole-body scans were performed 4 days after the application of radioiodine. The mean interval between two consecutive treatment courses was 4.6 months.

3.3. Results of treatment

In 191 of 209 children, more than one course of radioiodine treatment has been performed in Germany up to now. In those cases, the results of treatment could be checked by follow-up with I-131 scintigraphy (Fig. 2), ultrasonography of the neck, X-ray of the thorax and determinations of thyroglobulin in serum (Table 2).

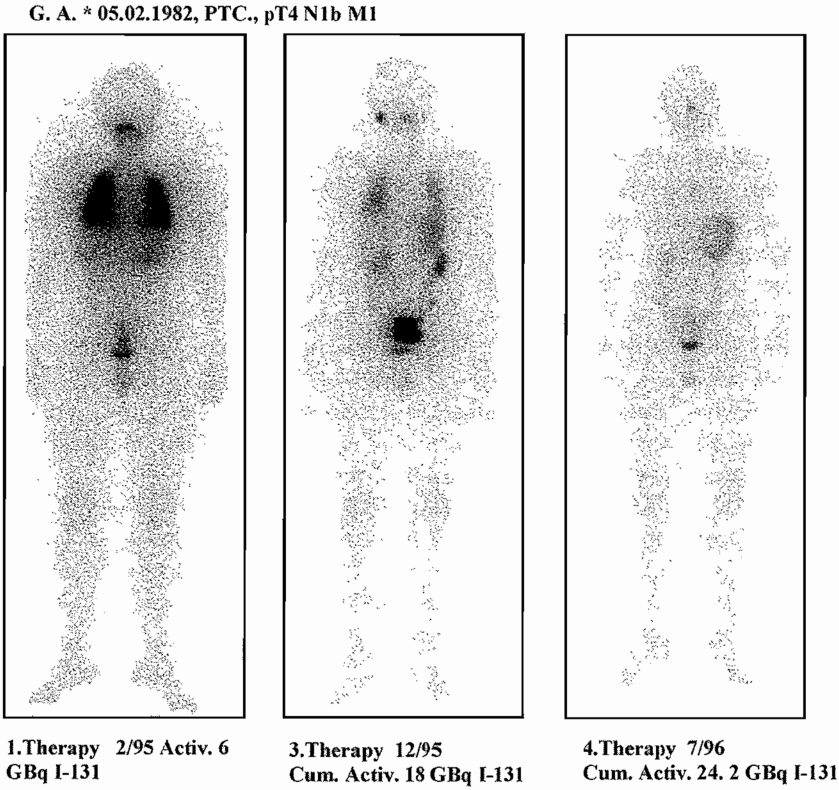

Fig. 2. I-131 whole-body scans in a 13-year-old boy with disseminated pulmonary metastases of papillary thyroid cancer successfully treated with four courses of radioiodine.

In 160 out of 191 children (84%), complete remissions of thyroid cancer could be achieved up to now. In 16%, we were able to recognize partial remissions defined as decrease of tumor volume, tumor marker serum level or intensity of radioiodine uptake for

Table 2
Results of radioiodine treatment in 191 children with differentiated thyroid cancer from Belarus (01.04.1993–31.12.2000)

N = 191			Complete remission	Partial remission	No change	Progressive disease
pT1–3	N0	M0	1	–	–	–
		M1	1	1	–	–
	N1	M0	35	1	–	–
		M1	4	11	–	–
pT4	N0	M0	1	–	–	–
		M1	1	–	–	–
	N1	M0	64	–	–	–
		M1	52	19	–	–

at least 50%. Fortunately, in no case progressive disease has been observed. It is important to mention that the results given here are not the final results of treatment since in some cases without complete remission, further courses of radioiodine are applicable. Up to now, fortunately, only three children from Belarus with thyroid cancer after Chernobyl died, among them, two cases with postoperative complications due to locally widespread tumor and one child with a recurrence which escaped from follow-up.

4. Discussion and conclusions

There is no doubt that exposure to radiation may induce thyroid cancer in children [1,5,6,9–27]. According to the review of Ron et al. [20] "The thyroid gland in children has one of the highest risk coefficients of any organ and is the only with convincing evidence for risk at about 0.1 Gy." Linearity best describes the dose response in children exposed to radiation before age of 15. Risk decreases significantly with increasing age at exposure, with little risk apparent after age of 20. The excess relative risk seems to be higher for females than that for males [20].

Latent times between radiation exposure and development of thyroid cancer range between minimally 3–7 years and maximally 40–50 years. Between 10 and 15 years, a nadir of the statistical distribution may be presumed [23]. The relative incidence of thyroid cancer per 100 000 of children below age of 15 increased in Belarus from 0.1–0.3 cases between 1986 and 1989 to 4.0 cases in 1995. For comparison: According to figures from the USA [7,16,28] and data from the German Cancer Registries in Hamburg and the Saarland, incidences of thyroid cancer in children below age of 15 amount to approximately 0.3–0.5 cases per 100 000.

It has been claimed that malignant thyroid tumors after external irradiation typically present as papillary cancers in approximately 85% of the exposed children and adolescents [19,24,26]. However, Samaan et al. [22] showed, when comparing two cohorts of thyroid cancer patients with and without a history of head and neck irradiation as children, that the proportion of papillary cancers in those two cohorts was not different with 87% and 84%, respectively. This indicates that papillary histology per se is typical for thyroid cancer in childhood and adolescence. However, Samaan's study revealed with statistical significance that bilateral lobe involvement (51%) and cancer not limited to the thyroid gland (70%) seemed to be characteristic for radiation-induced thyroid cancer [22].

Table 3 compares recent multicentric studies on childhood thyroid cancer from Italy, France and Germany [18,29] to the statistical material which is available at the Centre for Thyroid Tumors in Minsk, Belarus, about 574 cases of childhood cancer diagnosed after the Chernobyl accident between 1986 and 1997 [2,3].

Table 3 proves that a high proportion of papillary histology is typical for thyroid cancer in children and adolescents [22]. However, in children exposed to irradiation from Belarus the percentage of papillary cancers is extremely high with 98% as compared to children from Italy and France (82%) and Germany (78%). In addition, the proportions of tumors with multicentric growth (33% versus 20%) and pT4 stage (45% versus 25% and 29%, respectively) are higher in children from Belarus. Lymph node involvement as well is more frequent in children from Belarus (68%) as compared to children from Italy and

Table 3
Thyroid cancer in children: data from Belarus in comparison to data from Italy, France and Germany

Study features	Belarus [3]	Italy and France [18]	Germany [29]
Number of children	574	369	114
Mean age	9.9 years	14.6 years	13.2 years
Female/male	1.5:1	2.5:1	2.4:1
Papillary histology	98%	82%	78%
Multicentric growth	33%	–	20%
pT4	45%	25%	29%
pN1	68%	54%	52%
pM1	16%	17%	25%

France (54%) or Germany (52%). An unequivocal difference of the frequency of distant metastases is not conceivable (16% versus 17% and 25% respectively). However, the data available from Belarus may underestimate the frequency of distant metastases because routine I-131 whole-body scans have been performed only in a small subgroup of the patients.

To summarise, characteristics of thyroid cancer in children exposed to Chernobyl fallout seem to be papillary histology and signs of aggressive growth. However, it cannot be ruled out completely that these peculiarities are related to the younger age of Chernobyl children (mean 9.9 years) as compared to the mean ages of children from Italy and France (14.6 years) and Germany (13.2 years), respectively (Table 3).

It is well known that papillary thyroid cancers tend to spread via the lymphatic pathway to the lungs [30]. Typically, this miliary type of disseminated pulmonary metastases may only be detected by whole-body scintigraphy and not by thorax X-ray [24], which was observed in 47% of our children with lung metastases. Eighty-six of the nine children from Belarus with secondaries to the lungs treated in Germany presented with disseminated pulmonary lesions. These could be removed completely by I-131 therapy in 67% of the children. In the remaining 33% of patients, partial remissions have been observed with decreasing intensity of radioiodine uptake and reduction of mostly extremely elevated thyroglobulin levels in serum. However, 8 of those 90 children with radioiodine uptake in lung metastases showed decreases of vital capacity, which has been measured routinely during therapy. Computed tomography proved that pulmonary fibrosis had developed. Lung fibrosis is one of the possible complications of high-dose radioiodine treatment in patients with pulmonary metastases of thyroid cancer. However, five of the eight cases diagnosed in our study had been treated previously with Bleomycin which itself is known to induce pulmonary fibrosis. Fibrosis may develop according to the literature in up to 10% of children with lung metastases [31].

However, generally, prognosis of thyroid cancer in children is reported to be excellent [14,16,22,28,32,34]. Children have a prognosis better than the adults. Even in cases of scintigraphically, persistent pulmonary metastases prognosis seems to be good [30,33]. Today, it is generally accepted that treatment guidelines for children and adults have to be identical [14,16,22,28,32,34]. Routine treatment has to include thyroidectomy, selective removal of positive lymph nodes and consecutive radioiodine treatment. Only in cases stage pT1 total thyroidectomy and subsequent radioiodine ablation of thyroid remnants are not mandatory because of the excellent prognosis of such tumors. However, it should be taken into consideration that a tumor diameter of 1 cm in a 10-year-old child with a thyroid volume of approximately 10 ml is relatively larger by a factor of 2 as compared to a tumor of same size in an adult with a thyroid volume of 20 ml [35].

References

[1] International Atomic Energy Agency, One decade after Chernobyl: summing-up the consequences of the accident, IAEA and WHO, Vienna, 1996.

[2] E.P. Demidchik, A. Mrochek, Yu. Demidchik, T. Vorontsova, E. Cherstvoy, J. Kenigsberg, V. Rebeko, A. Sugenoya, Thyroid cancer promoted by radiation in young people of Belarus (clinical and epidemiological features), in: G. Thomas, A. Karaoglou, E.D. Williams (Eds.), Radiation and Thyroid Cancer, World Scientific, Singapore, 1999, pp. 51–54.

[3] E.P. Demidchik, Personal communication, March 2000.

[4] O.E. Epsthein, Personal communication, March 2000.

[5] M. Tronko, T. Bogdanova, I. Komisarenko, S. Rybakov, A. Kovalenko, O. Epsthein, V. Oliynik, V. Tereshchenko, I. Likhtarev, I. Kairo, M. Chepurnoy, The post-Chernobyl incidence of childhood thyroid cancer in Ukraine, in: G. Thomas, A. Karaoglou, E.D. Williams (Eds.), Radiation and Thyroid Cancer, World Scientific, Singapore, 1999, pp. 61–69.

[6] A.F. Tsyb, Shakhtarin, E.F. Lushnikov, V.F. Stepanenko, V.P. Snykov, E.M. Parshkov, S.F. Trofimova, Development of cancer and non-cancer thyroid diseases in children and adolescents after the Chernobyl accident, in: G. Thomas, A. Karaoglou, E.D. Williams (Eds.), Radiation and Thyroid Cancer, World Scientific, Singapore, 1999, pp. 79–87.

[7] Surveillance, Epidemiology and End Results (SEER) Program of the USA 1973–1994, National Cancer Institute, Bethesda, 1998.

[8] S. Franceschi, P. Boyle, P. Maisonneuve, C. La Vecchia, A.D. Burt, D.J. Kerr, G.J. MacFarlane, The epidemiology of thyroid carcinoma, Crit. Rev. Oncog. 4 (1993) 25–52.

[9] P. Jacob, Thyroid cancer risk to children calculated, Nature 392 (1998) 31–32.

[10] W.F. Heidenreich, J. Kenigsberg, P. Jacob, E. Buglova, G. Goulko, H.G. Paretzke, E.P. Demidchik, A. Golovneva, Time trends of thyroid cancer incidence in Belarus after the Chernobyl accident, Radiat. Res. 151 (1999) 617–625.

[11] P. Jacob, Y. Kenigsberg, I. Zvonova, G. Goulko, E. Buglova, W.F. Heidenreich, A. Golovneva, A.A. Bratilova, V. Drozdovitch, J. Kruk, G.T. Pochtennaja, M. Balonov, E.P. Demidchik, H.G. Paretzke, Childhood exposure due to the Chernobyl accident and thyroid cancer risk in contaminated areas of Belarus and Russia, Br. J. Cancer 80 (1999) 1461–1469.

[12] P. Jacob, Y. Kenigsberg, G. Goulko, E. Buglova, F. Gering, A. Golovneva, J. Kruk, E.P. Demidchik, Thyroid cancer risk in Belarus after the Chernobyl accident: comparison with external exposures, Radiat. Environ. Biophys. 39 (2000) 25–31.

[13] S. Akiba, J. Lubin, E. Ezaki, E. Ron, T. Ishimaru, Y. Asona, Y. Shimizu, H. Kato, Thyroid cancer incidence among atomic bomb survivors in Hiroshima and Nagasaki 1958–1979, Technical Report TR 5-91, Radiation Effects Research Foundation, Hiroshima, Japan, 1991.

[14] M.E. Dottorini, A. Vignati, L. Mazzucchelli, G. Lomuscio, L. Colombo, Differentiated thyroid carcinoma in children and adolescents: a 37-year experience in 85 patients, J. Nucl. Med. 38 (1997) 669–675.

[15] B.J. Duffy, P. Fitzgerald, Thyroid cancer in childhood and adolescence, Report of 28 cases, J. Clin. Endocrinol. Metab. 10 (1950) 1296–1308.

[16] J.B. Gorlin, S.E. Sallan, Thyroid cancer in childhood, Endocrinol. Metab. Clin. North Am. 19 (1990) 649–662.

[17] P. Hall, L.E. Holm, Radiation-associated thyroid cancer—facts and fiction, Acta Oncol. 37 (1998) 325–330.

[18] F. Pacini, T. Vorontsova, E.P. Demidchik, E. Molinaro, L. Agate, C. Romei, E. Shavrova, E.D. Cherstvoy, Y. Ivashkevitch, E. Kuchinskaya, M. Schlumberger, G. Ronga, M. Filesi, A. Pinchera, Post-Chernobyl

thyroid carcinoma in Belarus children and adolescents: comparison with naturally occurring thyroid carcinoma in Italy and France, J. Clin. Endocrinol. Metab. 82 (1997) 3563–3569.
[19] C. Reiners, J. Biko, N. Kruglova, E.P. Demidchik, Therapy of thyroid carcinoma in children from Belarus after the Chernobyl accident, in: J. Nauman, D. Glinoer, L.E. Braverman, U. Hostalek (Eds.), The Thyroid and Iodine, Merck European Thyroid Symposium Warsaw 1996, May 16–18. Schattauer, Stuttgart, 1996, pp. 89–97.
[20] E. Ron, J.H. Lubin, R.E. Shore, K. Mabuchi, B. Modan, L.M. Pottern, A.B. Schneider, M.A. Tucker, J.D. Boice, Thyroid cancer after exposure to external radiation: a pooled analysis of seven studies, Radiat. Res. 141 (1995) 259–277.
[21] E. Ron, A.B. Schneider, External radiation and the thyroid cancer risk in humans, in: G. Thomas, A. Karaoglou, E.D. Williams (Eds.), Radiation and Thyroid Cancer, World Scientific, Singapore, 1999, pp. 5–12.
[22] N.A. Samaan, P.N. Schultz, N.G. Ordonez, R.C. Hickey, D.A. Johnston, A comparison of thyroid carcinoma in those who have and have not had head and neck irradiation in childhood, J. Clin. Endocrinol. Metab. 64 (1987) 219–223.
[23] R.E. Shore, Issues and epidemiological evidence regarding radiation-induced thyroid cancer, Radiat. Res. 131 (1992) 98–111.
[24] R.E. Shore, Human thyroid cancer induction by ionizing radiation: summary of studies based on external irradiation and radioactive iodines, in: A. Karaoglou, G. Desmet, G.N. Kelly, H.G. Menzel (Eds.), European Commission and the Belarus, Russian and Ukrainian Ministries on Chernobyl Affairs, Emergency Situations and Health: The Radiological Consequences of the Chernobyl Accident, European Commission, Brussels, 1996, pp. 669–675.
[25] D. Williams, Editorial: thyroid cancer and the Chernobyl accident, J. Clin. Endocrinol. Metab. 81 (1996) 6–8.
[26] T. Winship, R.V. Rosvoll, Thyroid carcinoma in childhood: final report on a 20 year study, Clin. Proc. Child Hosp. (Washington, DC) 26 (1970) 327–349.
[27] P.B. Zanzonico, Age-dependent thyroid absorbed doses for radiobiologically significant radioisotopes of iodine, Health Phys. 78 (2000) 60–67.
[28] C.R. Moir, R.L. Telander, Papillary carcinoma of the thyroid in children, Semin. Pediatr. Surg. 3 (1994) 182–187.
[29] J. Farahati, T. Parlowsky, U. Mäder, C. Reiners, P. Bucsky, Differentiated thyroid cancer in children and adolescents, Langenbeck's Arch. Surg. 383 (1998) 235–239.
[30] R. Vassilopoulou-Sellin, M.J. Klein, T.H. Smith, N.A. Samaan, R.A. Frankenthaler, H. Goepfert, A. Cangir, T.P. Haynie, Pulmonary metastases in children and young adults with differentiated thyroid cancer, Cancer 71 (1993) 1348–1352.
[31] C. Reiners, G. Perret, W. Sonnenschein, V. John-Mikolajewski, Radiation reactions to the lung after radioiodine therapy for thyroid cancer, in: Th. Herrmann, Chr. Reiners, O. Messerschmidt (Eds.), Strahlenschutz in Forschung und Praxis, Band 36, Gustav Fischer, Stuttgart, 1994, pp. 139–146.
[32] D. Danese, A. Gardini, A. Farsetti, S. Sciacchitano, M. Andreoli, A. Pontecorvi, Thyroid carcinoma in children and adolescents, Eur. J. Pediatr. 156 (1997) 190–194.
[33] A.M. Samuel, B. Rajashekharrao, D.H. Shah, Pulmonary metastases in children and adolescents with well-differentiated thyroid cancer, J. Nucl. Med. 39 (1998) 1531–1536.
[34] R. Vassilopoulou-Sellin, H. Goepfert, B. Raney, P.N. Schultz, Differentiated thyroid cancer in children and adolescents: clinical outcome and mortality after long-term follow-up, Head Neck 20 (1998) 549–555.
[35] J. Farahati, C. Reiners, E.P. Demidchik, Is the UICC/AJCC classification of primary tumor in childhood thyroid carcinoma valid? J. Nucl. Med. 40 (1999) 2125.

International Congress Series 1234 (2002) 215–219

Comparison of thyroid cancer incidence after the Chernobyl accident in Belarus and in Ukraine

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Abstract

Data on thyroid cancer cases operated in the period 1986–1999 among those born in Belarus and in Ukraine during the period 1968–1985 are analysed. Whereas the dependence of the total number of thyroid cancer cases on time after exposure is similar in the two countries, there are obvious differences in the dependencies on age at operation and on age at exposure. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Chernobyl; Thyroid cancer

1. Introduction

A large increase of the thyroid cancer incidence was observed in Belarus [1] and in the northern oblasts (regions) of Ukraine [2] among those who were children or adolescents during the Chernobyl accident. In both countries, special registries were set up to which all of the operated cancer cases among those born after 1 January 1968 have to be reported. Compared to the national cancer registries, a main advantage of these special registries is the information on the place of residence at the time of exposure, which is a necessary prerequisite to perform risk estimates. All of the cases in the registries were diagnosed by

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PII: S0531-5131(01)00622-7

local pathologists. In Belarus, many of the cancer cases were checked by international teams of pathologists [3]. In Ukraine, one third of the cases (543 cases) were verified by the Institute of Endocrinology and Metabolism of Ukraine and most of these cases, again, were checked by international teams of pathologists. The confirmation rate for the cancer diagnosis was in the order of 97%.

2. Thyroid cancer incidence in Belarus and in Ukraine

The thyroid cancer cases that have been reported to the national thyroid cancer registries for the birth cohort 1 January 1968 to 31 December 1985 and for the time interval of operation from 1 January 1986 to 31 December 1999 amount to 1292 in Belarus and to 1613 in Ukraine (Fig. 1). The birth cohort includes 2.7 million persons in Belarus, and 13 million in Ukraine. In Belarus, the annual incidences increased from about 10 cases per year in the period 1986–1988, over 100 cases in 1992 to 185 cases in 1999. The corresponding incidences in Ukraine were 20, 110 and 251 cases per year. According to recent estimates of the exposure-independent baseline incidence, about two third of the cases in Belarus [4] and about one third of the cases in Ukraine [5] are due to the Chernobyl accident.

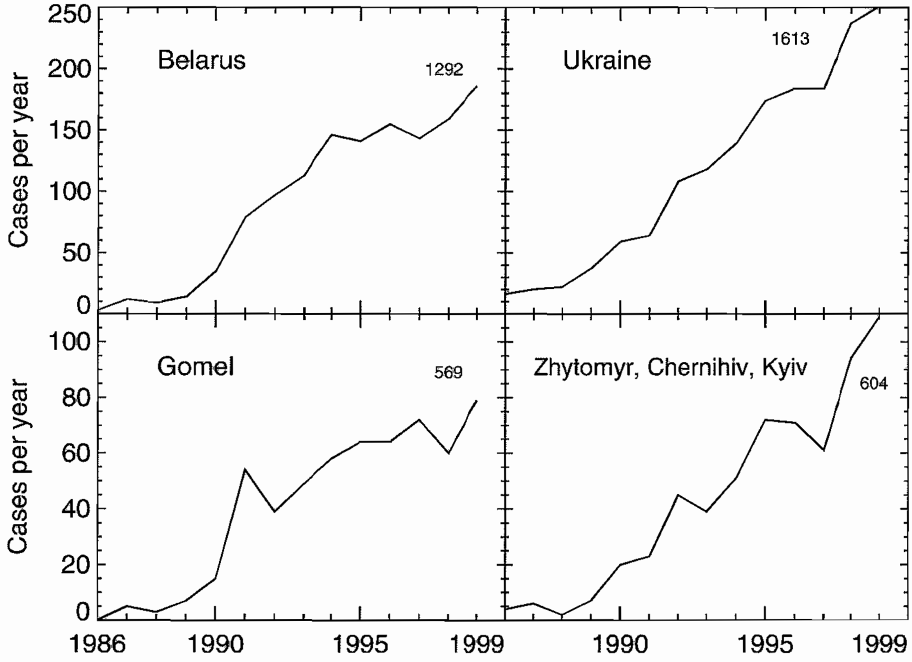

Fig. 1. Thyroid cancer cases that have been reported to the national thyroid cancer registries for the birth cohort 1 January 1968 to 31 December 1985 and for the time interval of operation from 1 January 1986 to 31 December 1999. The numbers in the figure give the cumulated number of cases.

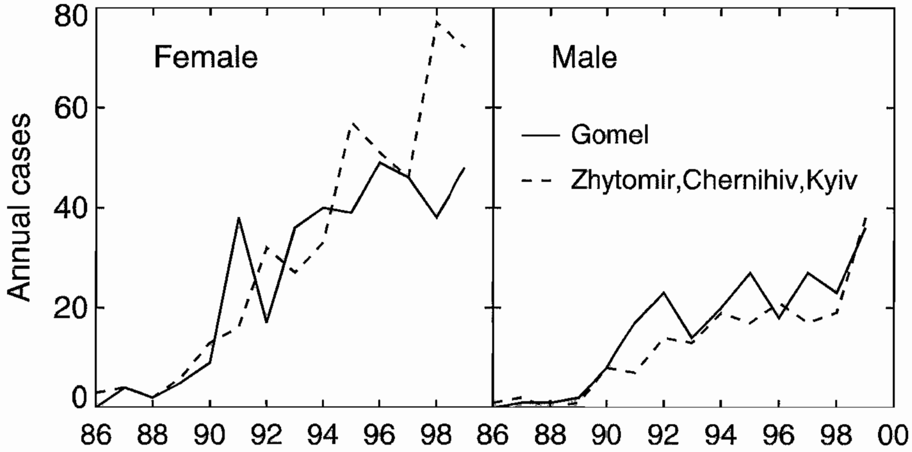

Fig. 2. Number of female and male thyroid cancer cases reported for the period 1986–1999 to the registries for the birth cohort 1968–1985 of Gomel oblast (0.24 million males and 0.23 million females) in Belarus and of the Zhytomyr, Chernihiv and Kyiv oblasts including Kyiv city (0.95 million males and 0.92 million females) in Ukraine.

Most of those born in 1986 were exposed in utero or by breast feeding. Their doses are smaller than those who consumed fresh milk. Among those born in 1986, 34 cases have been registered among 0.17 million Belorussian children and 31 cases among 0.77 million Ukrainian children. Accordingly, the thyroid cancer incidence rate among the 1986 birth cohort is 14 cases/10^6 person-years (PY) in Belarus (3 cases/10^6 PY in Ukraine) and

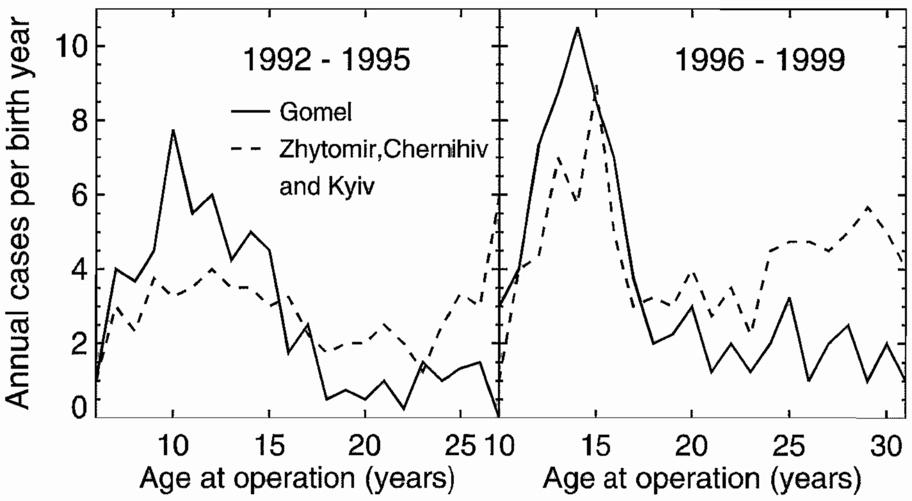

Fig. 3. Number of thyroid cancer cases as a function of age-at-operation as reported for the periods 1992–1995 and 1996–1999 to the registries for the birth cohort 1968–1985 of Gomel oblast in Belarus and of the Zhytomyr, Chernihiv and Kyiv oblasts including Kyiv city in Ukraine.

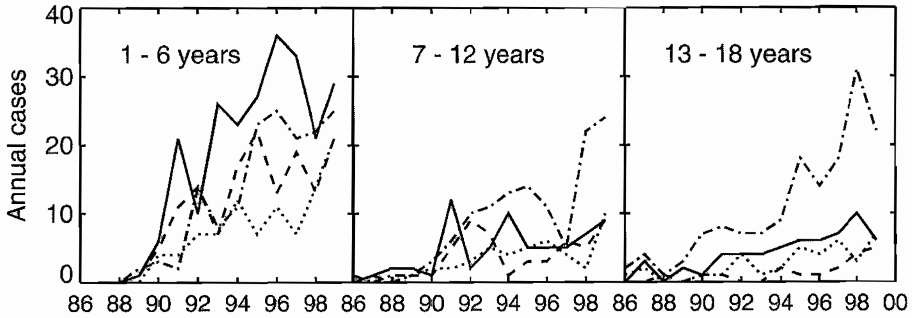

Fig. 4. Number of thyroid cancer cases reported for the period 1986–1999 to the registries for three birth cohorts of Gomel oblast in Belarus (solid line for females and broken line for males) and of the Zhytomyr, Chernihiv and Kyiv oblasts including Kyiv city in Ukraine (broken line with dots for females and dotted line for males).

considerably smaller than among the birth cohort 1968–1985 (34 cases/10^6 PY in Belarus and 8.9 cases/10^6 PY in Ukraine).

Radiation induced effects are especially expressed in highly contaminated regions. The living place at the time of the Chernobyl accident is used here to assign the cases to the different regions of the two countries. The lower panel of Fig. 1 shows operated thyroid cancer cases reported for the Gomel oblast (region) in Belarus and for the Zhytomyr, Chernihiv and Kyiv oblasts including Kyiv city in Ukraine. These areas have been chosen here to show dependencies of the thyroid cancer incidence on gender, on age-at-operation and on age-at-exposure.

In the contaminated areas of both countries, the ratio of the number of thyroid cancer cases among females is about a factor of 2 larger than among males (Fig. 2).

The thyroid cancer incidence in Gomel was highest for age at operation[1] of 10 years in the period 1992–1995 for age at operation of 14 years in the period 1996–1999 (Fig. 3). For older ages at operation (17–27 years in the period 1992–1995 and 21–31 years in the period 1996–1999), the number of cases does not vary strongly with age and the incidence in this age range is by factor of 6–8 smaller than in the peak. In the contaminated area of Ukraine, however, the incidence depends less on age at operation. An increase is observed for higher ages at operation, which is mainly due to an increasing incidence among females.

The incidence among those with an age at exposure[2] of 1–6 years is in Gomel by a factor of 5 larger than the incidence among those with an age-at-exposure of 13–18 years, the ratio of cases among females to cases among males is about the same in both age-at-exposure groups (Fig. 4). In the contaminated areas of Ukraine, the incidences in the two age-at-exposure groups differ less than by a factor of 1.5, the ratio of cases among females to cases among males is considerably larger for the older ones.

[1] Throughout the paper, the difference between the year of operation and the year of birth is used as a surrogate for the age at operation.

[2] Throughout the paper, the difference between 1986 and the year of birth is used as a surrogate for the age at exposure.

3. Conclusion

In summary, it may be concluded that the dependence of the total number of thyroid cancer cases on time after exposure is similar in the highly contaminated areas of Belarus and Ukraine. However, there are obvious differences in the dependencies on age at operation and on age at exposure. Probably, differences in screening and case reporting to the central registries contribute to these differences in the thyroid cancer incidence in the two countries. It may be concluded that thyroid cancer risk estimates based on these data [6–8] reflect situations as they can occur after exposures of larger population groups to ^{131}I and will therefore be of help in the planning of emergency actions like the distribution of the stable iodine in such a case.

Acknowledgements

This work was supported by the German Federal Office of Radiation Protection (BfS) under contract number StSch4240.

References

[1] V.S. Kazakov, E.P. Demidchik, L.N. Astakova, Thyroid cancer after Chernobyl, Nature 359 (1992) 21.
[2] I.A. Likhtarev, B.G. Sobolev, I.A. Kairo, N.D. Tronko, T.I. Bogdanova, V.A. Oleinic, E.V. Epshtein, V. Beral, Thyroid cancer in the Ukraine, Nature 375 (1995) 365.
[3] D. Williams, A. Pinchera, A. Karaoglou, K.N. Chadwick. Thyroid cancer in children living near Chernobyl. Expert panel report on the consequences of Chernobyl accident. Report EUR15248EN, European Commission, Brussels, 1993.
[4] P. Jacob, Y. Kenigsberg, G. Goulko, E. Buglova, A. Golovneva, J. Kruk, E.P. Demidchik, Thyroid cancer in Belarus after the Chernobyl accident: comparison with external exposures, Radiat. Environ. Biophys. 39 (2000) 25.
[5] V. Shpak, I. Likhtarev, I. Kairo, T. Bogdanova, N. Tronko, Reconstruction of thyroid dose and thyroid cancer risk in children and adolescents in Ukraine after Chernobyl accident, Proceedings of Ninth Symposium on Chernobyl-Related Health Effects, Radiation Effects Association, Tokyo, 2000, pp. 28–47.
[6] P. Jacob, Y. Kenigsberg, I. Zvonova, G. Goulko, E. Buglova, W.F. Heidenreich, A. Golovneva, A.A. Drozdovitch, V. Drozdovitch, J. Kruk, G.T. Pochtennaja, M. Balonov, E.P. Demidchik, H.G. Paretzke, Childhood exposure due to the Chernobyl accident and thyroid cancer risk in contaminated areas of Belarus and Russia, Br. J. Cancer 80 (1999) 1461.
[7] J. Kenigsberg, E. Buglova, A. Golovneva, J. Kruk, Thyroid cancer risk in Belarus after Chernobyl accident: reconstruction of individual thyroid dose and thyroid cancer, Proceedings of Ninth Symposium on Chernobyl-Related Health Effects, Radiation Effects Association, Tokyo, 2000, pp. 69–86.
[8] I.A. Likhtarev, I.A. Kayro, V.M. Shpak, N.D. Tronko, T.I. Bogdanova, Radiation-induced and background thyroid cancer of Ukrainian children (dosimetric approach), Int. J. Radiat. Med. 3–4 (1999) 51.

International Congress Series 1234 (2002) 221–229

Ultrasound diagnosis of radiation-induced childhood thyroid cancer in Belarus: 10 years of practical experience

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Keywords: Ultrasound diagnosis; Childhood thyroid cancer; Ultrasonography

1. Introduction

Because of its superficial location, thyroid gland is ideally situated for high-frequency ultrasound examination. Nowadays, ultrasound examination of thyroid is recognized as the most useful radiological examination for screening and early diagnosis of nodular thyroid disease, thyroid cancer in particular. Initial clinical application of ultrasound in diagnosis of thyroid diseases was made by Fujimoto et al. [1] in 1967. Technical possibilities of the equipment used at that time did not allow the assessment of morphological organ structure because there was no gray-scale estimation in the real scale of time. It was only possible to detect the thyroid gland itself and differentiate solid nodules from cyst. The improvement in the ultrasonic diagnostic equipment in the 1970s and usage of high frequency probes increased sensitivity of this examination [2]. At present, ultrasound is used to distinguish diffused pathological processes from local ones, cystic formations from solid ones; conduct topic, and, in some cases, nosology diagnosis [3,4]. Besides using ultrasound examination, it is possible to measure the exact thyroid volume. This information is extremely important for dose calculation in radio-iodine therapy. Ultrasonography is particularly useful during follow-up to control the patients' response for suppressive L-thyroxin therapy. One of the most important applications of

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PII: S0531-5131(01)00611-2

ultrasound in thyroid diagnosis is fine-needle aspiration biopsy (FNA) guidance. Continuing improvements in image quality and development of more sophisticated Doppler techniques will lead to an increased role of ultrasound in clinical management of thyroid patients [5].

After the Chernobyl accident, there was a tendency to a considerable increase in the incidence of thyroid cancer in Belarus. The frequency of thyroid cancer in children from Belarus, Ukraine, and the southwestern part of Russia had been increasing since 1990. There is no doubt that systematic screening of the thyroid gland in children that started in the most contaminated regions in 1990 contributed to it. However, the increase in the number of carcinoma cases was considerably higher than it could be expected due to the implementation of screening alone. In Belarus, by the end of 2000, 710 children with thyroid carcinoma were operated. Of these cases, pT1 was diagnosed in 21.7%, pT2–3 in 41.1%, and pT4 in 37.2% of the patients. In 69% of the children, lymph node metastases have been observed during surgery (pN1). Distant metastases (pM1) were diagnosed postoperatively in 17% of the children.

An analysis showed that child thyroid carcinoma is more aggressive compared to that of the adult, and characterized by a high frequency of complications required after additional surgery. These particularities make the problem of early diagnosis of thyroid cancer one of the most important.

The paper aimed to show our results in clinical application of ultrasound examinations for early diagnosis of thyroid cancer in children of Belarus.

2. Materials and methods

All children with thyroid pathology (nodes and diffuse changes in the thyroid at ultrasonic scanning) were thoroughly examined in "Aksakovschina", the hospital of Research and Clinical Institute of Radiation Medicine and Endocrinology, to prove or disprove thyroid pathology. A fine-needle aspiration was performed for those patients who had thyroid nodes of more than 0.5 cm.

Since 1990, 122 cases of thyroid carcinoma in children have been diagnosed in the Aksakovschina Clinic and all these patients were involved in our study. The male/female ratio was 1:1.6, age, 6–16 years.

2-D ultrasound thyroid examination was performed with the ultrasonic real-time scanner, "Toshiba" SSA 240A (7.5 MHz sector probe) and Hewlett Packard "Image Point" (7.5 MHz linear probe). Both gray-scale and Power Doppler images were analyzed. Sonography was performed with the patient in the spine position with the neck slightly hyperextended.

Using 2-D ultrasound examination, thyroid volume (V) measurements were done by measuring the height (H), width (W), and length (L) of the thyroid lobes from two selected orthogonal scans (transverse and sagittal). Calculation of thyroid volume, as that of the corresponding ellipsoid, was done by Brunn et al. [6]: $V=H\times W\times L\times 0.479$. The volumes of the right and left lobes were added together to give the total volume.

During the Power Doppler examination, we detected a pattern of nodule vascularisation. Power Doppler patterns of thyroid node vascularisation were classified into three

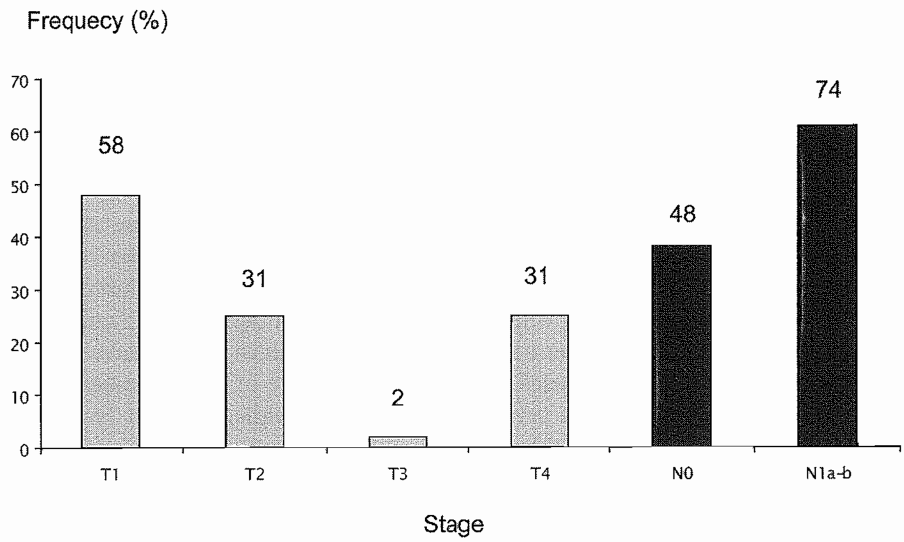

Fig. 1. Classification of 122 thyroid cancer cases by pTNM staging. The figure on the bar indicates the number of cases.

types: I—nodules without vascularisation, II—nodules with perinodular vascularisation, III—nodules with intra- and perinodular vascularisation [7]. All cases of thyroid carcinoma were verified by morphological study after surgery.

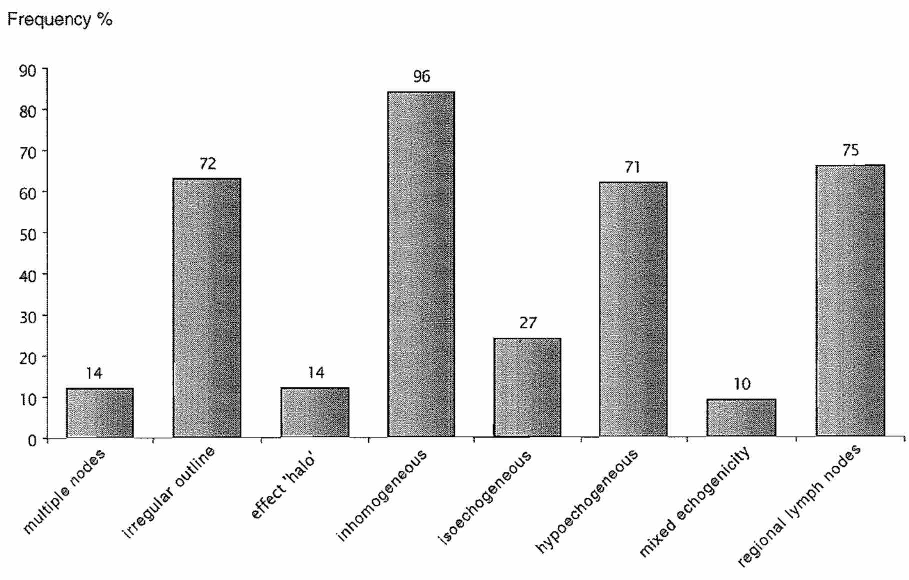

Fig. 2. Patterns of the ultrasound images of 114 thyroid carcinomas. The figure on the bar indicates the number of cases.

Statistical analysis was performed with parametric and nonparametric methods in the electronic tables Excel 5 of Microsoft Windows.

3. Results

The early recognition of thyroid carcinoma has become possible now due to the conducted mass ultrasonic screening and follow-up of patients from the risk group exposed to radiation (children exposed to ionising radiation in utero and during the first 4 years of their lives, and children with changes in the echoimage of the thyroid or with small nodules in thyroid in diameter up to 0.5 cm.) As a result of the intensive screening and follow-up program, we diagnosed patients with T1 stage of thyroid cancer (microcarcinoma) in 48.4% of our 122 patients (Fig. 1). Meanwhile, regional lymph node metastasis was found in 60.7% of the patients.

We have studied particularities of ultrasonic picture in thyroid cancer patients before surgical removal. Our experience showed that visualization of thyroid carcinoma is possible in two forms: nodular (114 patients—93.5%) and diffuse (8 patients—6.5%).

The nodular variant of thyroid carcinoma is visualized as a node that is located within the enlarged gland. The enlargement of the gland can be up to 1.5 times compared to the normal size of thyroid. Mean diameter of the nodules was 1.5 cm.

Patterns of the ultrasound images of thyroid cancer are shown in Fig. 2. Single node was registered in 88% of the cases. Two or more nodular formations were visible in 12% of the cases. The node was topically located next to the thyroid capsule in 95.5% of patients.

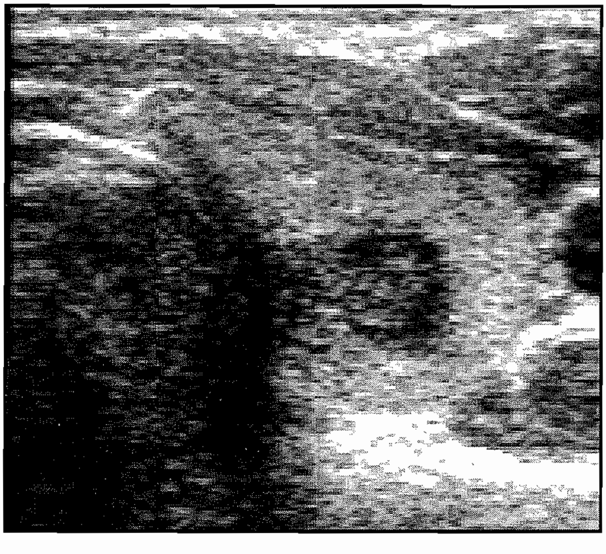

Fig. 3. Thyroid cancer with regular outline.

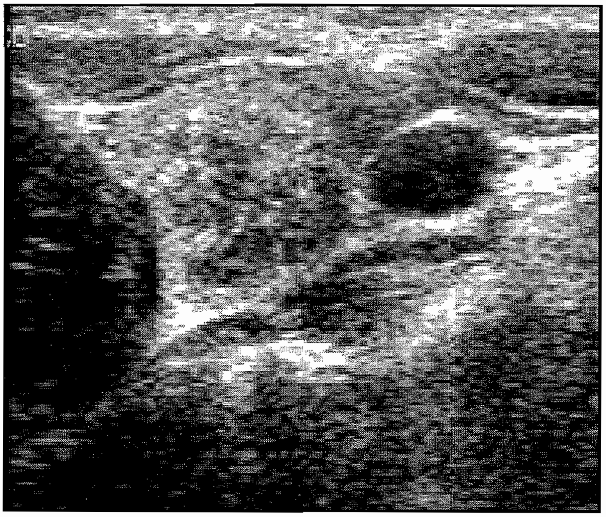

Fig. 4. Thyroid cancer with irregular outline.

The nodular formation looked more frequently like an inhomogeneous structure (84%) with both regular (37%) (Fig. 3) and irregular outline (63%) (Fig. 4). A "halo", a hypoechogenic margin, was observed in 12.4% of the children with thyroid cancer (Fig. 5). Thyroid nodes were hypoechogenic in the majority of the patients, 62% of the cases,

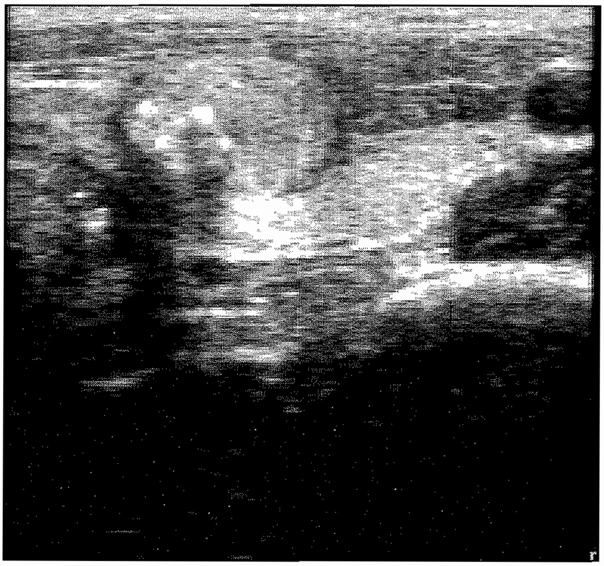

Fig. 5. Thyroid cancer with halo sign.

Fig. 6. Papillary carcinoma (T4N1M*x*). Multiple metastases in lymph nodes, (a) transverse scan, (b) longitudinal scan.

isoechogenic in 24%, and mixed in 14% of the cases. Pathological study showed that the isoechogenic feature of the node might indicate either the dissemination or multifocal growth of tumor within the thyroid gland [8].

In general, regional lymphatic nodes of different echogeneicity (hypo-, iso- and mixed) were visible in 66% of the children with the nodular form of thyroid cancer. By FNA, we proved that the isoechogenis pattern of lymph node visualization was typical for metastatic lymphatic nodes (Fig. 6).

The diffuse variant is characterized by essential volume enlargement of the thyroid (more than two times) with a diffuse structure modification, hypo- or mixed, inhomogenous echogeneicity (Fig. 7). Enlarged lymphatic nodes were visible in all cases. Although a hypoechogenic character of the thyroid was found in three out of eight children, mixed echogeneicity occurred more frequently (in five children). In the homogeneous and hypoechogenic character of the enlarged thyroid, children with the diffuse form of car-

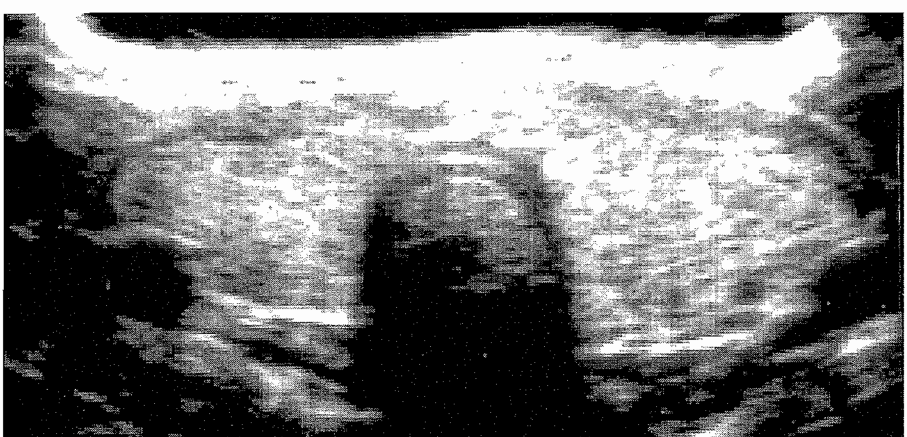

Fig. 7. Papillary carcinoma diffuse variant in transverse scan (looks like autoimmune thyroiditis) (T4N1BM0).

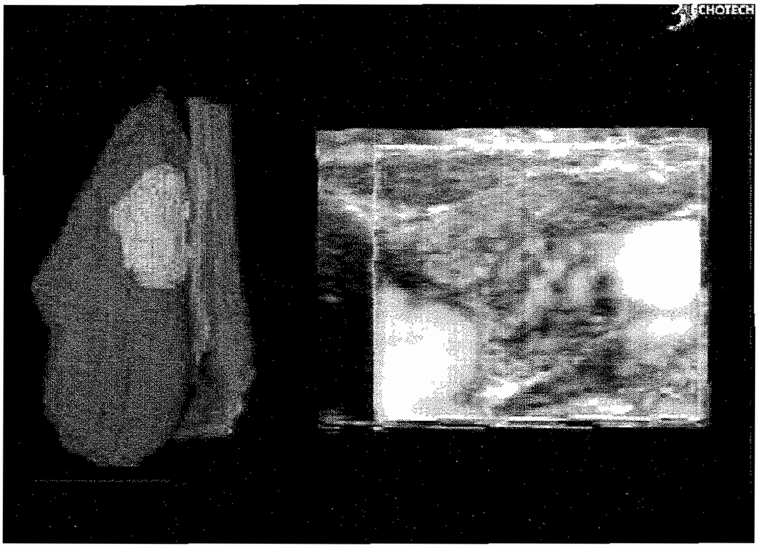

Fig. 8. 3-D reconstruction and Power Doppler images of thyroid carcinoma.

cinoma looked like an ultrasonic picture of autoimmune thyroiditis, and it was diagnosed only due to the fine-needle aspiration puncture.

Power Doppler examinations of the thyroid nodes were carried out in 11 thyroid cancer patients. Absence of intranodular vasularisation was registered only in three patients: type I of nodule vascularisation was registered in two patients, type II in one patient. Type III was registered much more often, in eight patients (Fig. 8).

4. Discussion

Nowadays, ultrasound plays a significant role in the early diagnosis of thyroid cancer. Particularities obtained in our study of ultrasound visualization of the thyroid carcinoma correspond to other reports. For example, 78% out of the 506 cases of thyroid carcinoma that were described from 1968 to 1983 were hypoechoic [9]. Besides, the most reliable ultrasound pattern of the nodular form the thyroid carcinoma in other reports was of an irregular outline [10,11].

In our study, ultrasound characteristics of thyroid carcinoma in children were more variable. For example, in 11.4% of the cases of thyroid carcinoma in children, we detected the "halo" sign. Therefore, in contrast to some authors [12], we cannot rely on the absence of "halo" as the good sign of malignancy.

In the current literature related to ultrasound investigations, we did not find any reference on the diffuse variant of thyroid carcinoma. The majority of authors analyze ultrasound images only for the nodular form of cancer with regular and irregular outline [13,14]. In children exposed to radiation, we observed the diffuse variant of thyroid carcinoma. This diffuse form may result from the multifocal growth and rapid progression of the disease. In some cases, diffuse forms were caused by diffuse sclerosing variant of papillary thyroid carcinoma.

One of the most important parts of ultrasound examination of children with thyroid carcinoma is the determination of affected regional lymph nodes. According to the pathological study, up to 18.2% of the cases of thyroid microcarcinoma [15] and 38–90% of all the cases of thyroid carcinoma are associated with regional lymph node metastasis [16]. Detection of multiple isoechogenic lymph nodes is one of the most reliably and frequently unique criteria for the early diagnosis of thyroid carcinoma metastasis. Criteria for ultrasound diagnostic of differentiation of benign and malignant lymph nodes in children are similar to those in adults [17].

Increased sensitivity in detecting slow blood flow using Power Doppler Sonography, in contrast to Color Doppler, enables to improve the detection of intranodal vascularity. As thyroid cancer growth is associated with tumor neoangiogenesis and neovascularisation [18], a high percentage of Power Doppler pattern III was more often found in children with thyroid malignancy than in children with benign nodes [12].

Future development of ultrasound diagnostics will be in the clinical application of the 3-D reconstruction of US images. This method can provide much more exact volume measurements, detailed topic diagnostics of node location, and its relation with surrounding tissues. Our experience in this sphere is unique, but our results fully correspond to the in vitro study on cadaver thyroids and phantoms [19,20], 3-D reconstruction allows to conduct a comparison of the ultrasound and morphological composition of the tumor. It could result in the improvement of early ultrasound verification of thyroid cancer.

5. Conclusion

Ultrasonic particularities of thyroid carcinoma in children exposed to radionuclides could be characterized as follows;

1. The ultrasonic picture of thyroid carcinoma, with respect to spread, can be distinguished into two forms: nodular and diffuse. The nodular variant can be divided into nodes with the limited spread (which have either regular or rather regular outlines) and nodes with a vast spread (with an irregular outline).

2. More frequently, the tumor is visualized as a hypoechogenic node. However, the isoechogenic feature of the node might indicate either the dissemination or multifocal growth of the tumor within the thyroid gland or diffuse sclerosing variant of papillary thyroid carcinoma.

3. Thyroid carcinoma is frequently followed by metastasis in regional lymph nodes. Isoechogenic character of visualized cervix lymph nodes is likely to indicate the presence of malignancy in the thyroid.

4. Location of the node next to the thyroid capsule might cause extra capsule dissemination of tumor (T4).

5. Recent improvement of early diagnosis of thyroid cancer increases a part of the patients with T1 stage and decreases T4.

6. 3-D ultrasound and Power Doppler Sonography could improve the early diagnosis of thyroid nodular pathology.

References

[1] Y. Fujimoto, A. Oka, R. Omoto, M. Hirose, Ultrasound scanning of the thyroid gland as a new diagnostic approach, Ultrasonics 5 (1967) 177–180.

[2] D.S. Ross, Evaluation of thyroid nodule, J. Nucl. Med. 32 (1991) 2181–2192.

[3] C.J. Garcia, A. Daneman, K. McHugh, et al., Sonography in thyroid carcinoma in children, Br. J. Radiol. 65 (1992) 977–982.

[4] F.N. Tessler, M.E. Tublin, Thyroid sonography: current applications and future directions, AJR Am. J. Roentgenol. 173 (2) (Aug. 1999) 437–443.

[5] K.S. Naik, R.F. Bury, Imaging the thyroid, Clin. Radiol. 53 (1998) 630–639.

[6] J. Brunn, U. Block, G. Ruf, et al., Volumetrie der Schilddrusenlappen mittels Real-time-Sonographie, Dtsch. Med. Wochenschr. 106 (41) (1981) 1338–1340.

[7] R. Lagalla, G. Caruso, M. Romano, M. Midiri, V. Novara, F. Zappasodi, Echo-color Doppler in thyroid disease, Radiol. Med. (Torino) 85 (5 Suppl. 1) (1993) 109–113.

[8] Chr. Reiners, V.M. Drozd, E.D. Cherstvoy, E.P. Demidchik, A.M. Nerovnya, M. Luster, Ultrasonography of the Thyroid in Children and Adolescents: Sonographic and Pathological Studies in a Population from Belarus After the Chernobyl Accident, Schattauer, Stuttgart, 2000.

[9] W. Wiedemann, Sonographie und Szintigraphie der Schilddruse: Lehrbuch und Atlas, Verlag, Stuttgart, 1993.

[10] L.A. Loevner, Imaging of the thyroid gland, Semin. Ultrasound CT MR 17 (6) (1996) 539–562.

[11] G.W. Gooding, Sonography of the thyroid and parathyroid, Radiol. Clin. North Am. 31 (1993) 967–973.

[12] T. Rago, P. Vitti, et al., Role of conventional ultrasonography and color flow-doppler sonography in predicting malignancy in "cold" thyroid nodules, Eur. J. Endocrinol. 138 (1998) 41–46.

[13] D. Lorenz, G. van Kaick, Echographische Diagnostik bei Erkrankungen der Schilddruse und der Nebenschilddruse, Rontgenpraxis 34 (1881) S315–S323.

[14] Chr. Reiners, I. Sieper, G. Simons, Schilddrusendiagnostik, Behringwerke, Germany, 1994, p. 143S.

[15] W. Lang, H. Borrusch, L. Bauer, Ocult carcinomas of thyroid: evaluation of 1020 sequential autopsies, Am. J. Clin. Pathol. 90 (1988) 72–76.

[16] D. Hay, Papillaty thyroid carcinoma, Endocrinol. Metab. North Am. 19 (1990) 719–739.

[17] P. Vassalo, K. Wernecke, N. Roos, P.E. Peters, Differentiation of benign from malignant superficial lymphadenopathy: the role of high-resolution US, Radiology 183 (1992) 215–220.

[18] J. Folkman, Tumor angiogenesis: role in regulation of tumor growth, Symp. Soc. Dev. Biol. 30 (1974) 43–52.

[19] E. Werner, S. Schloegl, J. Terechova, M. Lassmann, Chr. Reiners, Accuracy of the volumetric of the thyroid by 3D ultrasound: suitability for epidemiological studies? Results of a post mortem study, in: Endocrinologia Japonica, vol. 47, Suppl. 12-th International Thyroid Congress, p. 157.

[20] D. King, M. Shao, Evaluation of in vitro measurement accuracy of three-dimensional ultrasound scanner, J. Ultrastruct. Med. 10 (1991) 77–82.

International Congress Series 1234 (2002) 231–237

Ultrasound examination of thyroid diseases in children and adults living in Tula region of Russia

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Abstract

A medical team consisting of 36 specialists has examined 36 454 children and adults living in Tula region of Russia, where Cs-137 ground contamination levels are from 3.2 to 5.6 Ci/km^2. A procedure of ultrasound thyroid screening was divided to medical and computer parts. The medical part included registration through individual thyroid examination; ultrasound examination of the thyroid of each person; repeated ultrasound examination of individuals with thyroid abnormalities; fine-needle aspiration biopsy of the thyroid, if needed, under ultrasound guidance and blood drawing; and physical examination by endocrinologist. The "Chart of ultrasound screening" was elaborated to summarize ultrasound findings and to simplify the documentation. The computer-based information system assured: database maintenance; saving thyroid images in digital format; providing the patients with the results of their examinations; and obtaining health statistics data. In summary, in the group of 5–9 years of age, no thyroid carcinomas were found; in age group of 10–14 years — 0.013%; in age group of 15–19 years — 0.044%; in age group of 20–29 years — 0.091%; in age group of 30–39 years — 0.121%; in age group of 40–49 years — 0.553%; in age group of 50–59 years — 0.349%.

Keywords: Thyroid diseases; Ultrasound screening; Carcinoma; Chernobyl

1. Introduction

The conventional methods of medical examination for thyroid disease diagnosis begin with the inspection of patients by the endocrinologist. It should be realized, however, that the palpation and external inspection do not reveal all the thyroid diseases.

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PII: S0531-5131(01)00612-4

The principal difference in our ultrasound screening procedure compared with the conventional approaches was that it began with the primary ultrasound examination of the individuals by the ultrasonographists who concluded either normal thyroid state or thyroid abnormality.

In general, the medical part of ultrasound screening included five steps: (1) registration of the persons to be examined; (2) primary ultrasound examination of the thyroid of each person; (3) repeated ultrasound examination of individuals with abnormalities detected at previous step; (4) fine-needle aspiration biopsy of the thyroid abnormality, if needed, under ultrasound guidance and blood drawing; and (5) physical examination of patients by the endocrinologist.

The other part of the ultrasound screening was the collection and organization of data using computer-based information system. The "Chart of ultrasound screening" was elaborated to summarize ultrasound findings and to simplify the document filing by the medical team. The expert evaluation of the charts and the information from charts were entered into database. The computer-based information system assured: database keeping; saving thyroid images in digital format; providing the patients with detected thyroid diseases with the results of their examinations in the form of printed protocols; obtaining health statistics data and reports.

We have a 12-year experience of thyroid screening examinations using the above procedure. Twenty specialists of the medical part and 10 computer operators are capable to complete examination and data entry for 3000 persons within one working day.

2. Subjects and methods

Table 1 shows age and sex distribution of subjects examined. In all, 36 454 people underwent ultrasound screening examination. There were 16 238 (44.6%) males and 20 216 (55.4%) females. The main attention was given to children and teenagers. In the age group of 5–14 years, 23 936 (65.6%) persons were examined, in the age group of 15–19 years — 6754 (18.5%) persons, in the age group of 20–60 years or more — 5764 (15.9%) persons.

Table 1
Age and sex distribution of subjects examined

Age group	Total		Males		Females	
	No.	%	No.	%	No.	%
5–9	8958	24.57	4565	28.11	4393	21.73
10–14	14978	41.09	7576	46.66	7402	36.61
15–19	6754	18.53	2955	18.20	3799	18.79
20–29	1099	3.01	263	1.62	836	4.14
30–39	1647	4.52	332	2.04	1315	6.50
40–49	1810	4.97	316	1.95	1494	7.39
50–59	860	2.36	156	0.96	704	3.48
60–	348	0.95	75	0.46	273	1.35
All ages	36454	100.00	16238	100.00	20216	100.00

A total of 860 patients were examined with echo-guided fine-needle aspiration biopsy and cytologic investigation. Blood was taken from 266 patients to verify autoimmune thyroiditis. After screening, 74 patients underwent surgical operations.

The ultrasound images of the abnormal thyroid gland were saved in digital format or on thermopaper. On the basis of the screening results, a database was created.

The ultrasound screening program was carried out in the towns of Uzlovaya and Novomoskovsk of Tula Region. According to medical monitoring findings, Cs-137 ground contamination levels in Uzlovaya resulting from the accident at the Chernobyl Nuclear Power Plant were 3.2–5.6 Ci/km^2.

3. Results

On the basis of ultrasound examination, the following thyroid diseases were diagnosed: nodular goiter, multinodular goiter, solitary cyst, multiple cysts, autoimmune thyroiditis, and carcinomas. The diagnosis of diffuse goiter was established on the basis of qualitative and quantitative ultrasound criteria. However, those results are not presented in this paper because the data on ultrasound criteria of diffuse goiter are being developed separately.

Table 2 shows the frequency of nodular goiter and multinodular goiter, solitary and multiple cysts, autoimmune thyroiditis, and carcinomas in each age group. Thyroid abnormality was detected in 0.28% of 8958 patients of both sexes aged 5–9 years; in 1.68% of 14978 patients aged 10–14 years; in 4.13% of 6754 of patients aged 15–19 years; in 10.56% of 1099 patients aged 20–29 years; in 19.19% of 1647 patients aged 30–39 years; in 27.9% of 1810 patients aged 40–49 years; in 34.88% of 860 patients aged 50–59 years; and in 43.10% of 348 patients aged 60 years or more. Nodular and multinodular goiter was found in 0.28%, 0.68%, 4.13%, 10.56%, 19.19%, 27.4%, 34.88% and 43.10%, respectively. Solitary and multiple cysts were detected in 0.08%, 0.79%, 2.35%, 4.37%, 4.31%, 4.26%, 3.95% and 2.87%, respectively. Autoimmune thyroiditis was detected in 0.10%, 0.45%, 0.52%, 1.91%, 2.19%, 3.81%, 4.65% and 1.72%, respectively. In the group of 5–9 years, no thyroid carcinomas were found; in the group of 10–14 years they were detected in 0.013%; in the group of 15–19 years in 0.044%; in

Table 2
Frequency of thyroid diseases revealed in males and females by screening

Age group	Number of people examined	Nodular goiter		Multinodular goiter		Cyst		Cysts		Autoimmune thyroiditis		Carcinoma		Total	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
5–9	8958	6	0.07	2	0.02	4	0.04	4	0.04	9	0.10	—	—	25	0.28
10–14	14978	49	0.33	14	0.09	90	0.60	28	0.19	68	0.45	2	0.013	251	1.68
15–19	6754	68	1.01	14	0.21	111	1.64	48	0.71	35	0.52	3	0.044	279	4.13
20–29	1099	34	3.09	12	1.09	36	3.28	12	1.09	21	1.91	1	0.091	116	10.56
30–39	1647	124	7.53	83	5.04	51	3.10	20	1.21	36	2.19	2	0.121	316	19.19
40–49	1810	203	11.22	146	8.07	64	3.54	13	0.72	69	3.81	10	0.553	505	27.90
50–59	860	114	13.26	109	12.67	23	2.67	11	1.28	40	4.65	3	0.349	300	34.88
60–	348	51	14.66	83	23.85	7	2.01	3	0.86	6	1.72	—	—	150	43.10
All ages	36454	649	1.78	463	1.27	386	1.06	139	0.38	284	0.78	21	0.058	1942	5.33

Table 3
Frequency of thyroid diseases revealed in males by screening

Age group	Number of people examined	Nodular goiter		Multinodular goiter		Cyst		Cysts		Autoimmune thyroiditis		Carcinoma		Total	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
5–9	4565	2	0.04	–	–	3	0.07	1	0.02	3	0.07	–	–	9	0.20
10–14	7576	18	0.24	–	–	32	0.42	8	0.11	16	0.21	1	0.013	75	0.99
15–19	2955	15	0.51	3	0.10	27	0.91	12	0.41	4	0.14	–	–	61	2.06
20–29	263	4	1.52	1	0.38	5	1.90	1	0.38	1	0.38	–	–	12	4.56
30–39	332	11	3.31	6	1.81	7	2.11	3	0.90	2	0.60	1	0.301	30	9.04
40–49	316	20	6.33	11	3.48	7	2.22	2	0.63	1	0.32	1	0.317	42	13.29
50–59	156	11	7.05	4	2.56	4	2.56	1	0.64	–	–	–	–	20	12.82
60–	75	6	8.00	5	6.67	3	4.00	1	1.33	–	–	–	–	15	20.00
All ages	16238	87	0.54	30	0.18	88	0.54	29	0.18	27	0.17	3	0.019	264	1.63

the group of 20–29 years in 0.091%; in the group of 30–39 years in 0.121%; in the group of 40–49 years in 0.553%; and in the group of 50–59 years in 0.349%. With increasing age, the frequency of thyroid diseases showed a rise from 0.28% to 43.10%.

Among the various thyroid diseases, nodular and multinodular goiter were observed most frequently. With an increase in age, the respective frequency increased: from 0.07% to 0.02% at the age of 5–9 years; from 1.01% to 0.21% at the age of 15–19 years; from 14.66% to 23.85% at the age over 60 years.

The frequency of solitary cysts varied with age from 0.04% to 3.54%. At the age of 40–49 years, the frequency reached its maximum (3.54%), and at the age of 60 years or more, it decreased to 2.01%. Whereas, the frequency of nodular and multinodular goiter kept increasing with age, the frequency of cysts decreased after reaching its maximum. At the age of 60 years, the frequency of nodular and multinodular goiter exceeded that of cysts by six to seven times.

With an increase in age, the frequency of autoimmune thyroiditis increased from 0.10% at the age of 5–9 years to 4.65% at the age of 50–59 years, and then to 1.72% at the age of 60 years or more.

Table 4
Frequency of thyroid diseases revealed in females by screening

Age group	Number of people examined	Nodular goiter		Multinodular goiter		Cyst		Cysts		Autoimmune thyroiditis		Carcinoma		Total	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
5–9	4393	4	0.09	2	0.05	1	0.02	3	0.07	6	0.14	–	–	16	0.36
10–14	7402	31	0.42	14	0.19	58	0.78	20	0.27	52	0.70	1	0.014	176	2.38
15–19	3799	53	1.40	11	0.29	84	2.21	36	0.95	31	0.82	3	0.079	218	5.74
20–29	836	30	3.59	11	1.32	31	3.71	11	1.32	20	2.39	1	0.120	104	12.44
30–39	1315	113	8.59	77	5.86	44	3.35	17	1.29	34	2.59	1	0.076	286	21.75
40–49	1494	183	12.25	135	9.04	57	3.82	11	0.74	68	4.55	9	0.602	463	30.99
50–59	704	103	14.63	105	14.91	19	2.70	10	1.42	40	5.68	3	0.426	280	39.77
60–	273	45	16.48	78	28.57	4	1.47	2	0.73	6	2.20	–	–	135	49.45
All ages	20216	562	2.78	433	2.14	298	1.47	110	0.54	257	1.27	18	0.089	1678	8.30

Tables 3 and 4 present the frequency of thyroid diseases in males and females, respectively. As shown in the two tables, any thyroid disease occurred more frequently in females than in males. For example, in females aged 40–49 years, nodular goiter occurred in 12.25% while it occurred in 6.33% in males. Multinodular goiter was found in 3.48% of males and in 9.04% of females of the same group, solitary cysts in 2.22% and 3.81%, respectively, multiple cysts in 0.63% and 0.74%, respectively, autoimmune thyroiditis in 0.32% and 4.55%, respectively.

Our screening program revealed 21 cases of thyroid carcinoma (3 males and 18 females). All the patients with carcinomas were operated on at the Medical Radiological Research Center, Russian Academy of Medical Sciences (MRRC RAMS). There were 17 papillary carcinomas, two medullar carcinomas, and two follicular carcinomas. The results of tumor-staging were as follows: stage T1, four cases; stage T2, 15 cases; stage T3, two cases. The size of carcinomas ranged from 7 to 60 mm, 10 mm in four cases, 20 mm in 11 cases, 30 mm in three cases, 40 mm and more in three cases. Sixteen patients had solitary carcinomas and five patients had multiple ones. Five patients showed metastases into lymph nodes of the neck.

Thus, no thyroid carcinoma was found in patients aged 5–9 years and in those aged over 60 years. The frequency of thyroid carcinoma increased from 0.013% to 0.553% among patients aged 10–49 years and decreased up to 0.349% in those aged 50–59 years.

4. Discussion

The frequency of thyroid diseases has been already reported by the representatives of different medical authorities: epidemiologists, diagnosticians, endocrinologists, surgeons, and pathologists [4–11]. A considerable part of works shows the frequency of carcinomas in children [12] and adults [3]. So, according to the data of some national registers [3], the mortality rate of thyroid carcinomas made up 1% of all the carcinomas. In the USA, new thyroid carcinomas are yearly found in 11 000 persons. Among children, thyroid carcinomas occur in 0.2–3.0% [1] and according to other authors [3] — in 1.75% of patients aged up to 20 years. The frequency of thyroid carcinomas is higher in girls aged 10–20 years.

The frequency of thyroid diseases depends, in many respects, on the diagnostic method. So, during palpation nodular, formations were detected in 1.9–6.5% of cases examined. According to the data of some surgical clinics, nodular goiter occurred in 9–39% and carcinomas in 2–7%. Fine-needle aspiration biopsy can reveal 10% of carcinomas. During autopsy, some abnormal changes in the thyroid were noted in 91.62% and malignant lesions in 8.38%.

Ultrasound examination being notable for a high sensitivity [10] is used in increasing frequency for detection of any mass or tumor lesions in thyroid gland. According to the data using ultrasonographic findings, thyroid diseases are found in 27.3–67.0%.

The difficulty of epidemic evaluations is due not only to the method of examination. The incidence of thyroid diseases is influenced by sex, age, race, genetic factors, iodine deficiency, and classification used at the present moment.

A special attention among factors of the external and internal environment must be paid on exposure to radiation. This problem is especially urgent in the context of the Chernobyl accident [2,5–7,9] and nuclear weapon tests [8].

Within one month, ultrasound screening examinations of the thyroid were performed on 36454 individuals. There were 16238 (44.6%) males and 20216 (55.4%) females.

Different types of thyroid diseases were detected in males and females with different frequency in different age groups. Thyroid diseases were detected in 0.28% of 8958 patients aged 5–9 years; in 1.68% of 14978 patients aged 10–14 years; in 4.13% of 6754 of patients aged 15–19 years; in 10.56% of 1099 patients aged 20–29 years; in 19.19% of 1647 patients aged 30–39 years; in 27.4% of 1810 patients aged 40–49 years; in 34.88% of 860 patients aged 50–59 years; and in 43.10% of 348 patients aged 60 years or more. With increasing age, the frequency of thyroid diseases showed a sharp rise from 0.28% to 43.10%. In females, any kind of thyroid diseases occurred more frequently than in males.

Among the diseases detected, nodular and multinodular goiter occurred the most often. At the age of 5–9 years, nodular and multinodular goiter were detected in 0.09%; at the age of 10–12 years in 0.42%; at the age of 15–19 years in 1.22%; at the age of 20–29 years in 4.18%; at the age of 30–39 years in 12.57%; at the age of 40–49 years in 10.29%; at the age of 50–59 years in 25.93%; and at the age of 60 years or more in 38.51%.

The frequency of solitary and multiple cysts was 0.08%, 0.79%, 2.35%, 4.37%, 4.31%, 4.26%, 3.95% and 2.87%, respectively.

The frequency of autoimmune thyroiditis was 0.10%, 0.45%, 0.52%, 1.91%, 2.19%, 3.81, 4.65% and 1.72%, respectively. From 50 to 59 years, frequency was increasing from 0.10% to 4.65% and from 60 years, it was reducing up to 1.72%.

No thyroid carcinoma was found in patients aged 5–9 years and in those aged over 60 years. The frequency of thyroid carcinoma increased from 0.013% to 0.553% in patients aged 10–49 years and decreased to 0.349% in those aged 50–59 years.

In summary, ultrasound screening of the thyroid gland revealed a high frequency of thyroid diseases in 36454 children and adults living in the Tula region of Russia. Based on our results and the approaches to thyroid examination, more accurate epidemiological study can be established around Chernobyl to further clarify the cause and effect relationship between the Chernobyl accident and thyroid diseases, especially carcinomas.

References

[1] S. Yamashita, Y. Shibata (Eds.), Chernobyl: A Decade, Elsevier, Amsterdam, 1997.

[2] I.I. Dedov, A. Tsyb, V. Omelchenco, E. Matveenko, V. Kandror, N. Goncharov, V. Parshin, M. Borovincova, V. Peterkova, Thyroid autoantibodies in children from area contaminated with radioactive materials after the Chernobyl accident, in: S. Nagataki, T. Mori, K. Torizuka (Eds.), Eighty Years of Hashimoto Disease, Int. Congr. Ser., vol. 1028, Elsevier, Amsterdam, 1993, pp. 521–524.

[3] A.S. Hundahi, I.D. Fleming, A.M. Fremgen, H.R. Menck, A national cancer data base report on 53856 cases of thyroid carcinoma treated in the U.S., 1985–1995, Cancer 83 (12) (1998) 2638–2648.

[4] P. Lind, W. Langsteger, M. Molnar, H.J. Gallowitsch, P. Mikosch, I. Omez, Epidemiology of thyroid diseases in iodine sufficiency, Thyroid 8 (1998) 1179–1183.

[5] F.A. Mettler, H.D. Royal, V.S. Parshin, et al., Administration of stable iodine to the population around the Chernobyl nuclear power plant, Radiol. Prot. 12 (1992) 156–165.

[6] F.A. Mettler, M.R. Wiliamson, V.S. Parshin, et al., Thyroid nodules in the population living around Chernobyl, J. Am. Med. Assoc. 268 (1992) 616–619.

[7] S. Nagataki, K. Ashizawa, S. Yamashita, Cause of childhood thyroid cancer after the Chernobyl accident, Thyroid 8 (2) (1998) 115–117.
[8] N. Takamura, S. Yamashita, H. Namba, G.Y. Alipov, M. Ito, K. Ashizawa, I. Sekine, M. Espenberova, B. Gusev, Need for investigation of thyroid disease around Semipalatinsk Nuclear Nesting Site, Kazakhstan, Thyroid 8 (1998) 635–636.
[9] A.F. Tsyb, V.S. Parshin, V.F. Stepanenco, Thyroid diseases after the Chernobyl accident, 8th European Congress of Radiology, Vienna, Austria, 1993 (Abstract).
[10] A.F. Tsyb, V.S. Parshin, G.V. Nestaiko, S. Yamashita, S. Nagataki, Ultrasound Diagnosis of Thyroid Diseases, Moscow, 1994, p. 332.
[11] C. Wang, L.M. Crapo, The epidemiology of thyroid disease and implications for screening endocrinology and metabolism, Clin. North Am. 26 (1) (1997) 189–218.
[12] S. Yamashita, S. Nagataki, Chernobyl and thyroid, Thyroid 5 (3) (1995) 153–154.

International Congress Series 1234 (2002) 239–244

Histological characterization of papillary thyroid carcinoma in children, adolescents and young adults in Russia after the Chernobyl accident

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Abstract

The purpose of the study was to analyze the histological features of post-Chernobyl papillary thyroid carcinoma (PTC) that occurred in children, adolescents and young adults living in radionuclide-contaminated territories of the Russian Federation. We reviewed the histological sections of thyroid carcinoma in 123 patients (39 males and 84 females) aged 0–16 years at the time of accident from Bryansk, Kaluga, Oriol and Tula regions of Russia. All patients were surgically treated in the Clinic of Medical Radiological Research Center, Russian Academy of Medical Sciences during 1990–2000. The age range of patients at the time of surgery was 8–29 years. Papillary thyroid carcinoma was diagnosed in 109 cases (89%), follicular carcinoma in 10 (8%), medullary carcinoma in 4 (3%). In 54% of papillary thyroid carcinomas, the age of patients during the accident was 0–4 years. The classic papillary architecture of papillary thyroid carcinomas (or dominant papillary component) occurred in 25%; dominant follicular architecture in 46%; dominant solid in 11%. Twelve percent of tumors had mixed architecture without dominant architectural component. Diffuse sclerosing and other variants occurred in 6%. We analyzed the histological features of papillary thyroid carcinomas depending on the age of patients at accident (analyzed groups of 0–4 and 5–16 years), age at operation (groups of 8–14, 15–19 and 20–29 years) and the duration of a latent period (analyzed groups of 4–10 and 11–14 years). No significant differences of papillary thyroid carcinoma architecture depending on the patient's age at accident and on a duration of latent period have been revealed. We found that the occurrence of classic papillary architecture (or dominant papillary component) of papillary thyroid carcinoma often occurred in the 20–29 years age group at operation (33%) than in the 8–14 years age group (16%). © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Chernobyl; Thyroid carcinoma; Histology

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PII: S0531-5131(01)00613-6

1. Introduction

The histological study of thyroid carcinoma in children and adolescents after the Chernobyl accident revealed that papillary thyroid carcinoma (PTC) is a dominant type of thyroid malignant tumor, accounting for 96.5% in Belarus [1] and 92.9% in the Ukraine [2]. Post-Chernobyl PTCs in children from the Ukraine are mostly represented by tumors of solid-follicular architecture (79.8%) than PTCs in unexposed population of children from England and Wales in whom solid-follicular type occurred (33%) [3]. Belarussian authors [1] have demonstrated that architectural patterns of PTC depend on the time after exposure (latent period).

The aim of the present study was to analyze the histological features of post-Chernobyl PTCs that occurred in children, adolescents and young adults of Russia, and to compare our findings with those in Belarus and the Ukraine.

2. Materials and methods

A total of 123 cases of histological sections (39 males and 84 females) of thyroid carcinoma in children, adolescents and young adults (aged 8–29 years at the time of surgery) from Bryansk, Kaluga, Oriol and Tula regions of Russia were reviewed. All patients were surgically treated in the Clinic of the Medical Radiological Research Center, Russian Academy of Medical Sciences (MRRC RAMS) during 1990–2000. All cases of thyroid carcinoma were classified in accordance with the criteria of the WHO International Histological Typing of Thyroid Tumors [4].

3. Results

The 123 reviewed cases of thyroid carcinoma included 39 males and 84 females (M/F ratio 1:2.2). Among the patients, 81 (66%) came from Bryansk region, 19 (15%) from Kaluga, 19 (15%) from Tula, and 4 (4%) from Oriol region. Of the 123 patients, 109 (89%) had papillary thyroid carcinoma, 10 (8%) had follicular carcinoma, 4 (3%) had medullary carcinoma (Table 1). The 109 cases of papillary carcinoma included 34 males and 75 females (M/F ratio 1:2.2). The sex and age distributions of the patients at the time of the Chernobyl accident (April 26, 1986) are shown in Fig. 1. Three patients (two girls and one boy) were exposed in utero (6th (1) and 7th (2) months of pregnancy). The age of

Table 1
Classification of 123 thyroid carcinoma cases by histological type and age at the time of surgery

Histological type	Number of cases (%)	Age at surgery (years)		
		8–14 (%)	15–19 (%)	20–29 (%)
Papillary carcinoma	109 (89)	45 (96)	28 (88)	36 (82)
Follicular carcinoma	10 (8)	2 (4)	3 (9)	5 (11)
Medullary carcinoma	4 (3)	0	1 (3)	3 (7)
Total	123 (100)	47 (100)	32 (100)	44 (100)

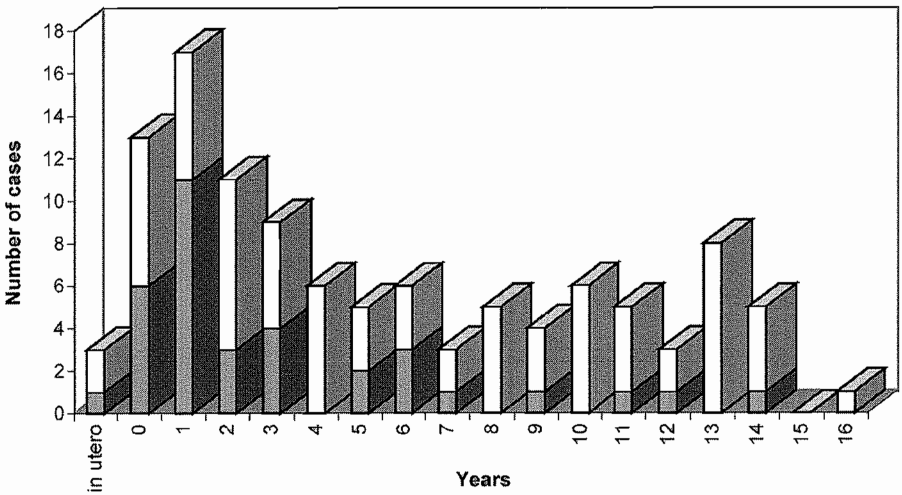

Fig. 1. Number of patients by sex and age at the time of the Chernobyl accident.

other 106 patients ranged from 2 months to 16 years. Of the 106 patients, 13 (6 boys and 7 girls) were younger than 1 year at the accident, the age of 93 patients (28 males and 65 females) ranged from 1 to 16 years. The age of 59 (54%) patients was 0–4 years at the time of the accident. The M/F ratio varied throughout the age groups. It was 1:1.4 in patients below 5 years of age compared to 1:4 in children 5–16 years at the time of the accident.

The distribution of cases by sex and age at the time of initial surgery is shown in Fig. 2. Their ages ranged from 8 to 29 years. The mean age for males was 15.3 and for females 18.3.

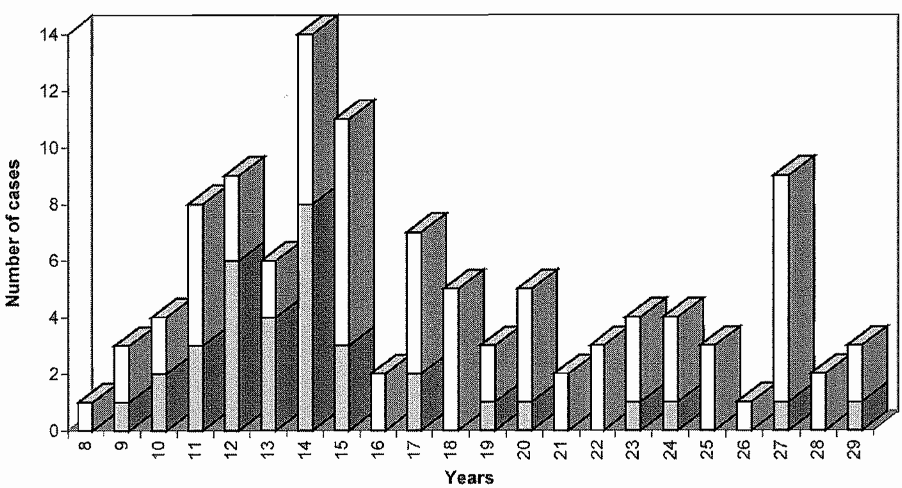

Fig. 2. Number of patients by sex and age at the time of surgery.

Table 2
Classification of 109 papillary thyroid carcinoma cases by architectural pattern and age (years) at the time of the accident

Architectural patterns	Number of cases (%)	Age at accident (M/F) (%)	
		0–4	5–16
Papillary dominant	27 (25)	12 (1:2) (20)	15 (1:6.5) (30)
Follicular dominant	50 (46)	30 (1:1.3) (51)	20 (1:5.7) (40)
Solid dominant	12 (11)	6 (1:1) (10)	6 (1:1) (12)
Mixed	13 (12)	8 (1:1) (14)	5 (1:1.5) (10)
Diffuse sclerosing variant	2 (2)	2 (0:2) (3)	0
Others	5 (4)	1 (0:1) (2)	4 (0:4) (8)
Total	109 (100)	59 (1:1.5) (100)	50 (1:4) (100)

There were 45 patients (24 males and 21 females, M/F ratio 1:0.9) in the 8–14 years age group, 28 patients (6 males and 22 females, M/F ratio 1:3.7) in the 15–19 years age group and 36 patients (6 males and 30 female, M/F ratio 1:5) in the 20–29 years age group.

The sex-specific distribution of age at the time of accident showed one prominent age peak for both males (0–1 year at the time of accident) and females (0–2 years at the time of accident) and one light age peak for female (13 years). The distribution of age at the time of surgery showed a similar pattern: there was one prominent age peak for both males (12–14 years at the time of surgery) and females (15 years) and one light peak for females (27 years at the time of surgery).

Papillary carcinomas showed a variety of histological appearances. They were assessed by their dominant architectural component: 27 cases (25%) were dominantly papillary, 50 (46%) dominantly follicular, 12 (11%) dominantly solid, 13 (12%) of tumors had mixed architecture without one dominant component. In addition, there were two tumors of diffuse sclerosing variant of papillary carcinoma, two tumors with morphology associated with familial polyposis coli and three papillary microcarcinomas. The distribution of architectural patterns of PTC by age of patients at the time of accident is shown in Table 2. There were light variations in the frequency of different architectural pattern of PTCs but they were not statistically significant. The distribution of architectural patterns of PTC by age of the patients at surgery is shown in Table 3. The occurrence of papillary carcinoma with classic papillary patterns (or dominant papillary component) in patients aged 20–29

Table 3
Classification of 109 papillary thyroid carcinoma cases by architectural pattern and age (years) at surgery

Architectural patterns	Number of cases (%)	Age at surgery (M/F) (%)		
		8–14	15–19	20–29
Papillary dominant	27 (25)	7 (1:0.8) (16)	8 (1:7) (28)	12 (1:11) (33)
Follicular dominant	50 (46)	22 (1:0.8) (49)	11 (1:4.5) (39)	17 (1:3.3) (47)
Solid dominant	12 (11)	6 (1:1) (13)	3 (1:0.5) (11)	3 (1:2) (8)
Mixed	13 (12)	9 (1:0.8) (20)	2 (1:1) (7)	2 (0:2) (6)
Diffuse sclerosing variant	2 (2)	1 (0:1) (2)	1 (0:1) (4)	0
Others	5 (4)	0	3 (0:3) (11)	2 (0:2) (6)
Total	109 (100)	45 (1:0.9) (100)	28 (1:3.7) (100)	36 (1:5) (100)

Table 4
Classification of 109 papillary carcinoma cases by architectural pattern and latent period (years)

Architectural patterns	Number of cases (%)	Latent period (M/F) (%)	
		4–10	11–14
Papillary dominant	27 (25)	7 (1:0.8) (20)	20 (1:9) (27)
Follicular dominant	50 (46)	13 (1:3) (38)	37 (1:1.6) (49)
Solid dominant	12 (11)	6 (1:1) (18)	6 (1:1) (8)
Mixed	13 (12)	5 (1:1.5) (15)	8 (1:1) (11)
Diffuse sclerosing variant	2 (2)	1 (0:1) (3)	1 (0:1) (1)
Others	5 (4)	2 (0:2) (6)	3 (0:3) (4)
Total	109 (100)	34 (1:1.8) (100)	75 (1:2.3) (100)

years at operation was more common (33%) than in patients of 8–14 years at operation (16%). No significant difference of architectural patterns of PTC between other age groups was revealed. The distribution of architectural patterns of PTC depending on the duration of a latent period is shown in Table 4.

4. Discussion

In our study, we examined the histological features of post-Chernobyl PTCs in patients who were children and adolescents at the time of the accident. These individuals were children (41%), adolescents (26%) and young adults (33%) at the time of surgery. PTC was diagnosed in 89% of the whole group. However, among children (8–14 years at operation) PTC was diagnosed in 96%. This figure is higher than that reported in England and Wales [3] and close to the figure reported among Belarussian [1] and Ukranian children [2]. The age distribution of the cases at the time of surgery showed a slightly bell-shaped curve. The peak incidence at the age of 11–12 was also demonstrated in Belarus and Ukraine. The histological patterns of PTC varied with age. Tumors with the papillary dominant pattern occurred more often in older patients (33%) than in young children (16%). Tumors with solid architectural pattern were more common in younger children (13%) than in older subjects (8%) but this difference was not significant in this study. Tumors with dominant solid and dominant follicular architecture were found in 61% cases in the group aged 8–14 years at surgery, in 50% cases in the group of 15–19 and in 55% cases in the group of 20–29 years at the time of surgery. The frequency of solid-follicular PTCs reported in the Ukraine [2] is higher (79.8% in children and 69.6% in adolescents). Our figures are intermediate between the frequency of solid-follicular subtype of PTC seen in England and Wales and that seen in the Ukraine. The high relative frequency of the solid-follicular type of PTC in children from exposed areas of Belarus and the Ukraine suggests that this type may be specifically associated with radiation. Belorussian authors [1] demonstrated that the architectural features of PTC depend on the duration of a latent period. More recently [5], studies carried out on Belorussian tissue specimens revealed differences in molecular genetic aberrations and the related phenotypes of PTCs occurred in the first post-Chernobyl decade. No differences of dominant architectural patterns of tumors depending on the duration of a latent period like that observed in Belarus have been revealed in our study. Possibly it was due to the differences of analyzed age groups, differences between the chronological periods chosen and a smaller number of examined cases in Russia.

References

[1] E. Cherstvoy, V. Pozharskaya, A. Nerovnya, The pathomorphology of childhood papillary thyroid carcinoma in Belarus in different periods after the Chernobyl accident (1991–1997), in: G. Thomas, A. Karaoglou, E.D. Williams (Eds.), Radiation and Thyroid Cancer, World Scientific, Singapore, 1999, pp. 55–60.
[2] T. Bogdanova, V. Kozyritsky, M. Tronko, I. Likhtarev, I. Kairo, M. Chepurnoy, V. Shpak, Morphological features and analysis of radiation risk of development of post-Chernobyl thyroid carcinoma in children and adolescents of Ukraine, in: G. Thomas, A. Karaoglou, E.D. Williams (Eds.), Radiation and Thyroid Cancer, World Scientific, Singapore, 1999, pp. 151–154.
[3] H.R. Harach, E.D. Williams, Childhood thyroid cancer in England and Wales, Br. J. Cancer 72 (1995) 777–783.
[4] Ch. Hedinger, E.D. Williams, L.H. Sobin, Histological typing of thyroid tumours, International Histological Classification of Tumours, 2nd edn., Springer, WHO, Berlin, 1988.
[5] H.M. Rabes, E.P. Demidchik, J.D. Sidorov, E. Lengfelder, C. Beimfohr, D. Hoelzel, S. Klugbauer, Pattern of radiation-induced RET and NTRK1 rearrangements in 191 post-Chernobyl papillary thyroid carcinomas: biological, phenotypic, and clinical implications, Clin. Cancer Res. 6 (2000) 1093–1103.

International Congress Series 1234 (2002) 245–252

Influence of the Chernobyl accident on thyroid function and non-tumor morbidity

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Abstract

We summarized the results of studies on the post-Chernobyl thyroid function among evacuees from the estrangement zone, "liquidators" of 1986 period and people living for a long time ("self-settlers") and working in the 30-km zone. Studies were conducted using standardized procedures including clinical examination, thyroid ultrasound examination, and assay of serum thyroid hormones and anti-thyroid antibodies content. Both of the radiation exposure modes, e.g., short-term, prolonged, combined, and the radiation dose were taken into account in the analysis of the results. The data analyzed indicated that the thyroid function has been subjected to alteration through the post-Chernobyl period and that nonstochastic radiation effects on the thyroid function, i.e., chronic thyroiditis and hypothyroidism, have been emerging though gradually.

Keywords: Chernobyl disaster; Ionizing radiation; Thyroid gland; Nonstochastic effects; Chronic thyroiditis; Hypothyroidism

1. Introduction

Incomparable release of radioactive iodine to environment as a result of the Chernobyl Nuclear Power Plant accident (11.8–12.0 million Ci of ^{131}I without taking short-lived isotopes into account) predetermined the leading type of health consequences, especially thyroid diseases [1].

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PII: S0531-5131(01)00614-8

Early and severe stochastic effects of irradiation on thyroid gland, i.e., malignant tumors in children and adolescents, have been observed after the Chernobyl accident for the first time. This evidence completely drew attention of researchers to that problem, leaving almost no interest to the nonstochastic thyroid aftermath, e.g., chronic thyroiditis and hypothyroidism. Both benign diseases, however, are not less important than malignant tumors from the viewpoint of the integral health detriment.

Thyroid dosimetry data indicate the inevitability of the increase in these diseases among various people affected by the accident. According to the published data, in addition to the liquidators and evacuees from the 30-km zone around the Chernobyl Nuclear Power Plant, 185 000 Ukrainian residents received the thyroid irradiation dose exceeding 0.3 Gy including 28 000 who received more than 1 Gy.

A clear dependence of absorbed dose on the age of affected people was observed: the younger in age, the more the dose was. Thus, children aged 0–3 years at the time of the accident received the highest thyroid dose.

Analysis of literature data regarding the effects of radioactive iodine on thyroid makes it worth paying attention to the fact that low dose of radionuclides did not lead to hypothyroidism although functional and organic alterations in the gland were pronounced.

Significant corrections by age were done for radiation effects on the thyroid gland. Experimental exposure of adult animals to radioactive iodine revealed the increased incidence of degenerative effects followed by glandular parenchyma necrosis and fibrosis [2,3]. In young animals, the thyroid injuries arose under lower doses than in adults but the capacity for functional compensation (hormone production ability) was preserved for a longer period by means of compensatory thyroid hyperplasia. The autoimmune processes take an important place in the pathogenesis of nonstochastic radiation effects on the thyroid gland. Studies on survivors of the Hiroshima and Nagasaki atomic bombings indicate the potential genesis of hypothyroidism on the autoimmune thyroiditis [4,5].

2. Subjects and methods

The present work summarizes the results of examinations conducted within post-Chernobyl period by the clinic of Research Center for Radiation Medicine, Academy of Medical Sciences of Ukraine. The subjects were 23 182 persons belonging to various population contingents of the Chernobyl disaster [6–10]. A total of 6179 (1869 children and 4310 adults) were examined in the clinic, while the remaining of 17 003 (12 499 children and 4504 adults) were examined within 30-km zone around the Chernobyl Nuclear Power Plant and in contaminated territories.

The cohorts studied were as follows:

1. children of various age including those irradiated in prenatal period, adults evacuated from the estrangement zone, and residents of territories contaminated with radionuclides;
2. liquidators of the consequences of the Chernobyl Nuclear Power Plant disaster including people who worked for a long time (not less than 5 years) in the 30-km estrangement zone around the Chernobyl Nuclear Power Plant; and

3. unauthorized residents of the 30-km zone, i.e., the "self-returnees" to estrangement zone.

For comparison, residents of Kiev city with similar age were examined, and as the control group, people from "clean" districts of the Poltava region were examined.

The thyroid study program included clinical examination, thyroid ultrasound examination and assay of serum thyroid hormones content.

In the clinical examination stage, the standardized data processing computer system for clinical thyroid screening was used [11].

Immunological research included the immunogram of serum immunoglobulin with the assay of anti-thyroglobulin and anti-microsome antibodies.

Table 1
Total serum thyroxin (T_4) content (nmol/l) among children and adults in the first year after the Chernobyl Nuclear Power Plant accident

Age (years) at the time of the accident	Statistical indices[a]	Time (months) since the Chernobyl Nuclear Power Plant accident			
		6	8	10	12
0–3	N	38	49	36	42
	Mean±SD	251.9±11.8	151.2±10.5	109.5±4.0	143.0±12.6
	P	<0.001	<0.01	<0.01	<0.01
	P_4	<0.01	>0.05	>0.1	<0.01
4–6	N	64	70	83	34
	Mean±SD	245.1±8.5	141.4±8.9	106.3±3.5	137.9±14.2
	P	<0.001	<0.01	<0.05	<0.01
	P_1	>0.1	>0.1	>0.1	>0.1
	P_4	<0.01	>0.1	>0.1	<0.01
7–10	N	124	220	162	253
	Mean±SD	210.2±6.1	131.0±4.0	107.1±2.8	128.6±8.1
	P	<0.001	<0.01	<0.02	<0.01
	P_1	<0.01	>0.05	>0.1	>0.1
	P_2	<0.01	>0.1	>0.1	>0.1
	P_4	=0.05	>0.1	>0.1	<0.01
11–15	N	147	214	253	158
	Mean±SD	188.4±5.5	113.2±3.9	95.4±2.0	108.9±4.5
	P	<0.001	<0.01	>0.1	<0.02
	P_1	<0.01	<0.01	<0.01	<0.02
	P_2	<0.01	<0.02	<0.02	=0.05
	P_3	<0.02	<0.01	<0.01	<0.05
	P_4	>0.1	>0.1	>0.1	<0.01
Adults	N	21	25	26	17
	Mean±SD	172.7±18.8	121.3±15.9	104.1±13.0	85.8±4.7
	P	<0.001	>0.05	>0.1	>0.05
Control	Mean±SD	91.3±5.1			

[a] N=Number of subjects; SD=standard deviation; P=significance probability of the difference as compared to control; P_1=significance probability for the difference as compared to the group of 0–3 years of age; P_2=significance probability for the difference as compared to the group of 4–6 years of age; P_3=significance probability for the difference as compared to the group of 7–10 years of age; P_4=significance probability for the difference as compared to the group of adults.

3. Results and discussion

We classified chronologically the results of research into three stages:

1. primary thyroid reaction;
2. latent preclinical period; and
3. period of clinical manifestation of thyroiditis.

Primary thyroid reactions to radiation exposure observed in 1986–1988 were hyperthyroxinemia and short-term elevation of thyrotropin content in blood. Total thyroxin level in blood showed a significant decrease with age (Table 1).

In the group of children with thyroid dose exceeding 2 Gy, a statistically relevant dose–response relationship was observed for total serum thyroxin content (Fig. 1).

Hormonal deviations at that stage had no clinical manifestation, which is thyroid morbidity in all age groups did not exceed the one in the preaccident period.

No substantial shifts in morbidity were observed in the subsequent period either (1989–1990).

In children assigned to the high risk groups, i.e., those evacuated from Pripyat city and resident of the most severely contaminated territories (Narodichi district of Zhitomir region) with thyroid radiation dose exceeding 0.3 Gy, the prevalence of hyperthyroxinemia remained in the period of 1988–1989. Among children with thyroid radiation dose under 0.3 Gy, the frequency of hyperthyroxinemia in the same period did not differ from that in the control.

In the study of cellular and humoral immunity among children in contaminated territories and those evacuated from Pripyat city, a decrease in the total content of T-

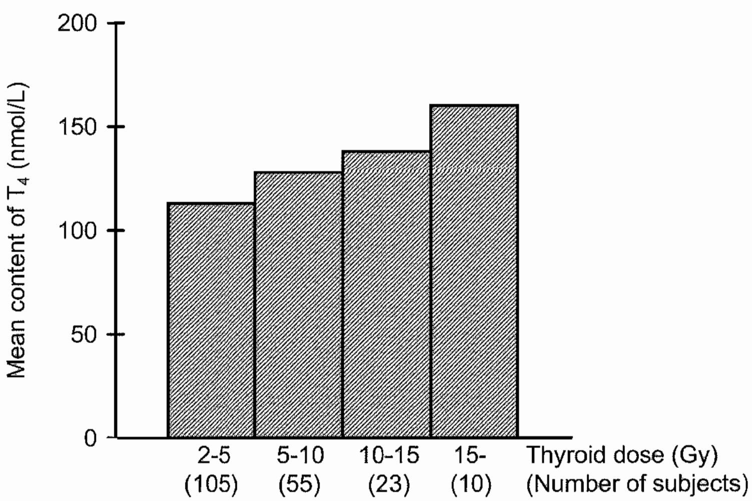

Fig. 1. Mean content (nmol/l) of total serum thyroxin (T_4) in children with thyroid dose exceeding 2 Gy. Measurement was conducted in the first year after the accident.

cells and their suppressor subpopulation was observed until 1989 as well as predominance of T-helper subpopulation. Serum immunoglobulin content did not differ from the normal level.

A significant correlation was observed between total serum thyroxin content and titers of anti-thyroglobulin antibodies in exposed children.

The above-mentioned immune disorders are the factors predisposing to autoimmune thyroid disorders.

Autoimmune processes were also predetermined by primary reaction of thyroid to radiation, i.e. euthyroid hyperthyroxinemia. Excessive content of total serum thyroxin in children after the accident was probably provided with its serum protein-bound fractions including the auto-antigen—thyroglobulin with normal content of free thyroxin. Excess in circulation of thyroglobulin could occur as the result of alteration in structure and function of thyroid cellular membranes in response to radiation exposure.

In the same period, a difference was observed between children from Narodichi districts and two districts of Poltava region (Mashevka and Lokhvitsa districts) through thyroid ultrasound examination. In some children living in contaminated areas, a high level of echogenic, echopositive and hydrophilic parts in thyroid tissues were observed. There are no such findings in children of the control group.

In the study of high risk groups, i.e., children exposed to radiation in prenatal period and people who worked for a long time or permanently reside in the 30-km zone around the Chernobyl Nuclear Power Plant, appropriate shifts demonstrating dose–response relationship for thyroid effects and the role of immune disorders in their genesis were observed.

However, no substantial disorder of endocrine systems including thyroid was observed in the period of 1991–1993 among children exposed to radiation in prenatal period. Nevertheless, a significant correlation was observed between thyroid radiation dose and serum thyrotropin content, which was within normal range at that stage. This may indicate the presence of interaction between prenatal thyroid exposure to radiation and the risk of thyroid dysfunction.

In permanent residents of the 30-km zone ("self-returnees"), a significant correlation was observed between serum thyroxin content, thyroid dose, and inhalation radiation dose (Table 2). We note that a significant correlation was observed between serum thyroxin content and titers of anti-thyroglobulin antibodies in the same group.

Table 2
Correlation between serum thyroid hormone content and radiation dose in 176 "self-returnees"

Hormone[a]	Thyroid dose	Effective equivalent dose	External gamma-radiation dose	Inhalation radiation dose	Internal radiation dose
TSH	−0.219	−0.229	−0.211	−0.216	−0.217
FT_4	0.333*	0.280	0.162	0.351*	0.282
ATG	−0.368	−0.306	−0.285	−0.348	−0.295

[a] TSH = thyroid stimulating hormone; FT_4 = free thyroxin; ATG = anti-thyroglobulin antibody.

* Correlation was significant at $P<0.05$.

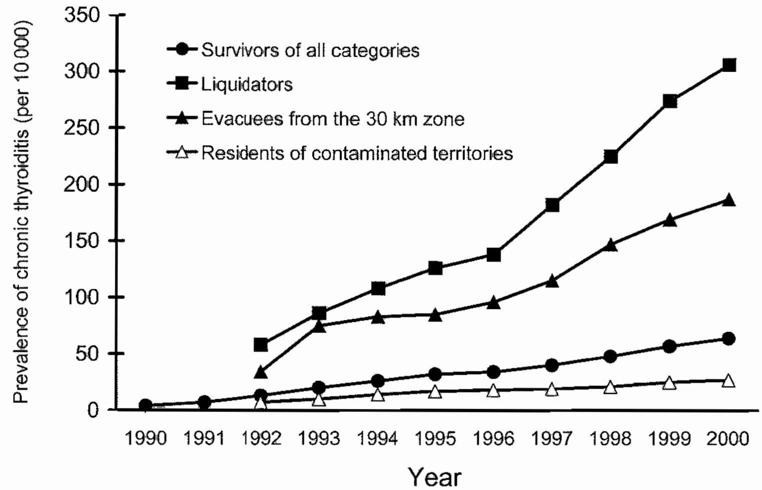

Fig. 2. Prevalence of chronic thyroiditis in adult and adolescent survivors of various categories (per 10 000 population).

Functional and structural alterations in the thyroid glands that were revealed in the period of 1986–1990 and were interacted with immune system disorders demonstrated their clinical manifestation, which began in the period of 1992–1993, through increasing prevalence of chronic thyroiditis and hypothyroidism among the survived population.

According to the official statistical data issued by Ministry of Health Protection of Ukraine [12–14], the occurrence of chronic thyroiditis per 10 000 population increased during the period of 1990–2000, from 4.0 to 63.8 among adult and adolescent survivors of

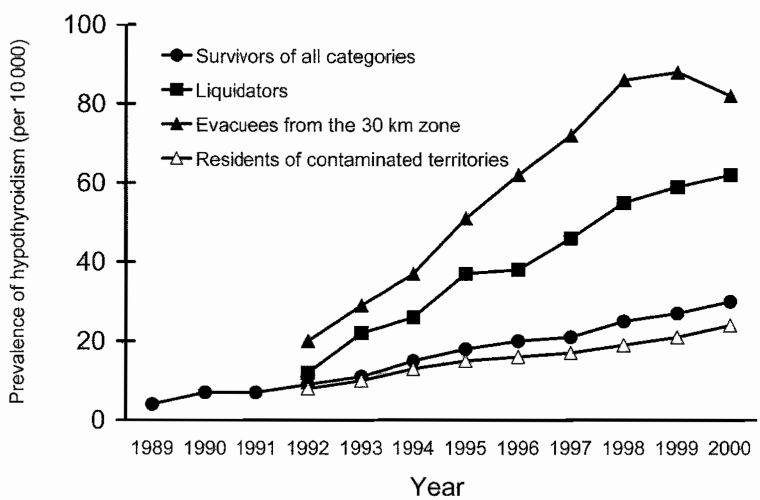

Fig. 3. Prevalence of hypothyroidism in adult and adolescent survivors of various categories (per 10 000 population).

all categories, to 306.1 among adult and adolescent liquidators, and to 187.7 among adult and adolescent evacuees from the 30-km zone (Fig. 2).

Similarly, the occurrence of hypothyroidism per 10 000 population increased during the period of 1989–2000, from 6.5 to 29.6 among adult and adolescent survivors of all categories, to 61.6 among adult and adolescent liquidators, and to 84.0 among adult and adolescent evacuees from the 30-km zone (Fig. 3).

4. Conclusions

The results of 15-year clinical survey provide a basis for objective conclusions regarding the nonstochastic thyroid consequences of the Chernobyl Nuclear Power Plant accident.

(1) Changes in thyroid function are marked characteristic of nonstochastic radiation effects on thyroid, which gradually progressed during all periods since the Chernobyl Nuclear Power Plant accident. Direct temporal link to radiation factor, dose-dependence and existence of dose threshold are characteristic features of nonstochastic radiation effects.

(2) Early primary functional thyroid reaction to radiation was observed in the first year after the accident, which manifested through "euthyroid" hyperthyroxinemia and short-term "stress" hyperthyrotropinemia followed by further interconnections with restoration in pituitary and thyroid axis system.

(3) Thyroid doses in survivors were positively dependent on age while the extent of hyperthyroxinemia was negatively dependent on age.

(4) Primary thyroid reaction to radiation, immune shifts in the first year after the accident and alterations in thyroid structure revealed by ultrasound examination, which began in 1990–1991, indicated with high probability the onset of autoimmune thyroiditis.

(5) Nonstochastic radiation effects on thyroid were dependent on thyroid dose and mode of radiation. Threshold dose at which radiation-induced effects were registered was about 30 cGy. Significant correlation between functional state of thyroid gland and individual radiation dose was marked in various study groups (children exposed in prenatal period, those with high thyroid dose and elderly people in the 30-km zone).

(6) Initial clinical forms of nonstochastic radiation effects on thyroid, i.e., chronic thyroiditis with hypothyroidism outcome became clearly apparent since 1992–1993. Results of clinical survey were validated by previous epidemiological data.

(7) Regarding various age-related adaptation and compensation capacities of organism in survivors, in contrast to thyroid cancer issue, the chronic thyroiditis and hypothyroidism occurred initially not only in children but also in the adult exposed population.

(8) A high risk group of chronic thyroiditis and hypothyroidism is also constituted of survivors with the most complex mode of thyroid irradiation, i.e., a combination of internal exposure to ^{131}I and short-lived iodine isotopes on the one side and external gamma-radiation on the other side. Females are concerned first of all among former residents of the 30-km zone around the Chernobyl Nuclear Power Plant and participants in liquidation of the consequences of the Chernobyl Nuclear Power Plant disaster in the "iodine period" of 1986.

(9) Nonstochastic radiation effects on thyroid, e.g., chronic thyroiditis with hypothyroidism outcome will further make a substantial contribution to thyroid morbidity in Chernobyl disaster survivors.

(10) Progress of thyroid disorders with time will have a substantial impact on organism of energy-supply system, especially on mechanism of adaptation and compensation for strain, which will affect the general psychosomatic morbidity. Participation of thyroid disorders and related integral disorders in endocrine regulation is possible in puberty period disorders (physical and sexual progress disorders), reproductive function and premature aging process.

References

[1] International Project on Health Effects of Chernobyl Disaster, Technical Report, Radiological consequences and protective arrangements estimates, IAEA, Vienna, 1992.

[2] L.A. Ilyin, Radioactive Iodine in Radiation Safety Problem, Atomizdat, Moscow, 1972.

[3] M. Alcardz, J. Meseguer, A. Garcia-Ayala, Effects of radiation on rabbit thyroid gland ultrastructure, J. Submicrosc. Cytol. Pathol. 22 (3) (1990) 433–440.

[4] S. Nagataki, Delayed effects of atomic bomb radiation on the thyroid, in: S. Nagataki (Ed.), Radiation and the Thyroid, Excerpta Medica, Tokyo, 1989, pp. 10–18.

[5] S. Nagataki, Y. Shibata, S. Inoue, et al., Thyroid diseases among atomic bomb survivors in Nagasaki, JAMA, J. Am. Med. Assoc. 272 (5) (1994) 364–370.

[6] A.K. Cheban, O.S. Dekhtyariova, O.V. Kopylova, et al., Thyroid function, structure and clinical characterization in children exposed to ionizing radiation after the Chernobyl Nuclear Power Plant accident: results of the first four years of survey, Pediatrics 12 (1991) 26–29.

[7] A.K. Cheban, A.E. Livkutnic, I.A. Ignatovskaya, I.G. Chikalova, Endocrine system in persons long time working in 30-km estrangement zone, in: Chernobyl-94. Presentations Collection from International Conference, Chernobyl, vol. 2 (1994) 32–45.

[8] A.K. Cheban, O.Y. Boyarskaya, V.G. Bebeshko, Thyroid condition in children after the Chernobyl accident, The Chernobyl Accident. Thyroid Abnormalities in Children, Congenital Abnormalities and Other Radiation Related Information. The First Ten Years, Hiroshima-Nagasaki Peace Foundation, 1996.

[9] A.K. Cheban, D.E. Afanasyev, O.Y. Boyarskaya, Some aspects of thyroid system status in persons exposed to the Chernobyl accident (IAEA-CN-67/18), Low doses of ionizing radiation: biological effects and regulatory control, IAEA-TECDOC-976, Contributed papers of International Conference, Seville, Spain, 17–21 November, IAEA, WHO, UNSCEAR, 1997, pp. 74–78.

[10] A.E. Romanenko, A.K. Cheban, O.S. Dekhtyareva, et al., The function, structure and clinical characteristics of thyroid in children exposed to irradiation following the Chernobyl accident, in: F. Pacini (Ed.), Open Problems of Human Radiobiology. The Post-Chernobyl, 1993, pp. 71–74, Pisa.

[11] A.K. Cheban, G.F. Limanskaya, Selection of thyroid risk groups in population wide-mass studies with Screening System "DIANA" application, Chernobyl Nuclear Power Plant Accident Health Consequences Radiation Epidemiology Problems, Proceedings of Scientific Conference, Kiev, 19–20 October 1993, pp. 310–314, Kiev.

International Congress Series 1234 (2002) 253–266

Cancer incidence in Belarus after the Chernobyl accident

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Abstract

This paper presents data on changes in cancer incidence in Belarus in the post-Chernobyl period. Average figures for the periods 1980–1989 and 1990–1999 were compared. Data for the whole Belarus, as well as for Gomel, Vitebsk and Minsk regions, are presented. The average annual increases in the crude incidence rate per 100 000 person-years (slope of linear regression) for the periods 1980–1989 and 1990–1999 were 9.89 (95% confidential interval: 9.2–10.59) and 9.14 (8.07–10.21) for males and 5.30 (4.75–5.84) and 7.75 (6.75–8.76) for females, respectively. The average annual increases in the age-standardized rate (ASR, world standard population) for the same periods were 7.98 per 100 000 (7.11–8.84) and 4.79 (4–5.59) for males and 3.18 (2.68–3.67) and 3.6 (3.1–4.11) for females, respectively. The 1980–1989/1990–1999 standardized rate ratio (SRR) for all cancers was: for males, in total, of Belarus, 1.24 (1.23–1.25), of the Gomel region, 1.37 (1.35–1.4), of the Minsk region, 1.28 (1.26–1.31); for females, in total, of Belarus, 1.23 (1.22–1.24), of the Gomel region, 1.32 (1.29–1.34), of the Minsk region, 1.28 (1.25–1.31). On the average, in Belarus, the most increase in ASR was observed for the following sites: for males, prostate 1.7 times, kidney 2.22 and thyroid 3.32; for females, kidney 2.2 and thyroid 4.07. A significantly higher increase in ASR was observed in separate regions than in Belarus in total: in the Gomel region, for males—in rectum and bladder cancers; for females—in bladder and thyroid cancers; in the Minsk region, for males and females—in leukemia.

Keywords: Cancer; Chernobyl; Incidence; Time trend; Belarus

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PII: S0531-5131(01)00615-X

1. Introduction

One of the expected consequences of the Chernobyl accident is an increase in cancer risk. Presently, the problem of the acute increase of thyroid cancer incidence in Belarussian, Ukrainian and Russian children exposed to ^{131}I is well known and studied. The objective of this paper was to study changes in the cancer incidence in Belarus in the post-Chernobyl period. Not pretending to reveal the relation of these changes with radiation exposure, the authors nevertheless counted it necessary to show the objective picture not just for the entire Belarus, but also for separate regions with different levels of radioactive contamination.

2. Material and methods

Data on incident cases registered from 1980 to 1999 in Belarussian Cancer Registry, which is population-based and covers the whole of Belarus, were used for this study. The data on the mean resident population from 1980 to 1999 up to region level were obtained from the Belarussian State Statistical Department.

Two decades, 1980–1989 and 1990–1999, were chosen for comparison. Both average crude rate (CR) and age-standardized incidence rate (ASR, world standard population) were calculated for each period. Data on changes in relative frequencies of the leading types of cancer were presented. To demonstrate changes in incidence, the 1980–1989/1990–1999 standardized rate ratio (SRR) was calculated. To estimate temporal changes in incidence growth, the average annual increase/decrease in CR and ASR per 100 000 person-years were calculated for each period using simple linear regression approximation. For reflecting the regional variations in the incidence time trends, data were presented both for the entire Belarus and for several regions: Gomel region as the most contaminated by radionuclides, Vitebsk region as "clean" and Minsk region as weakly contaminated were selected for the study.

All calculations were made using the formulas given in Ref. [1]. Data on changes in age-specific incidence rates were also presented.

3. Results and discussion

3.1. Changes in population structure

Fig. 1 shows average population structure (percentage) for the periods 1980–1989 and 1990–1999. It should be noted that in 1990–1999, proportion of the population aged 35–74, which contributes mostly to cancer incidence, slightly increased as compared to 1980–1989 (42.9% vs. 37.5% for males and 46.6% vs. 43.0% for females).

3.2. Relative frequency of leading cancers

In 1990–1999, certain changes in the relative frequency of different types of cancer were observed in Belarus as compared to the previous decade. Fig. 2 shows relative

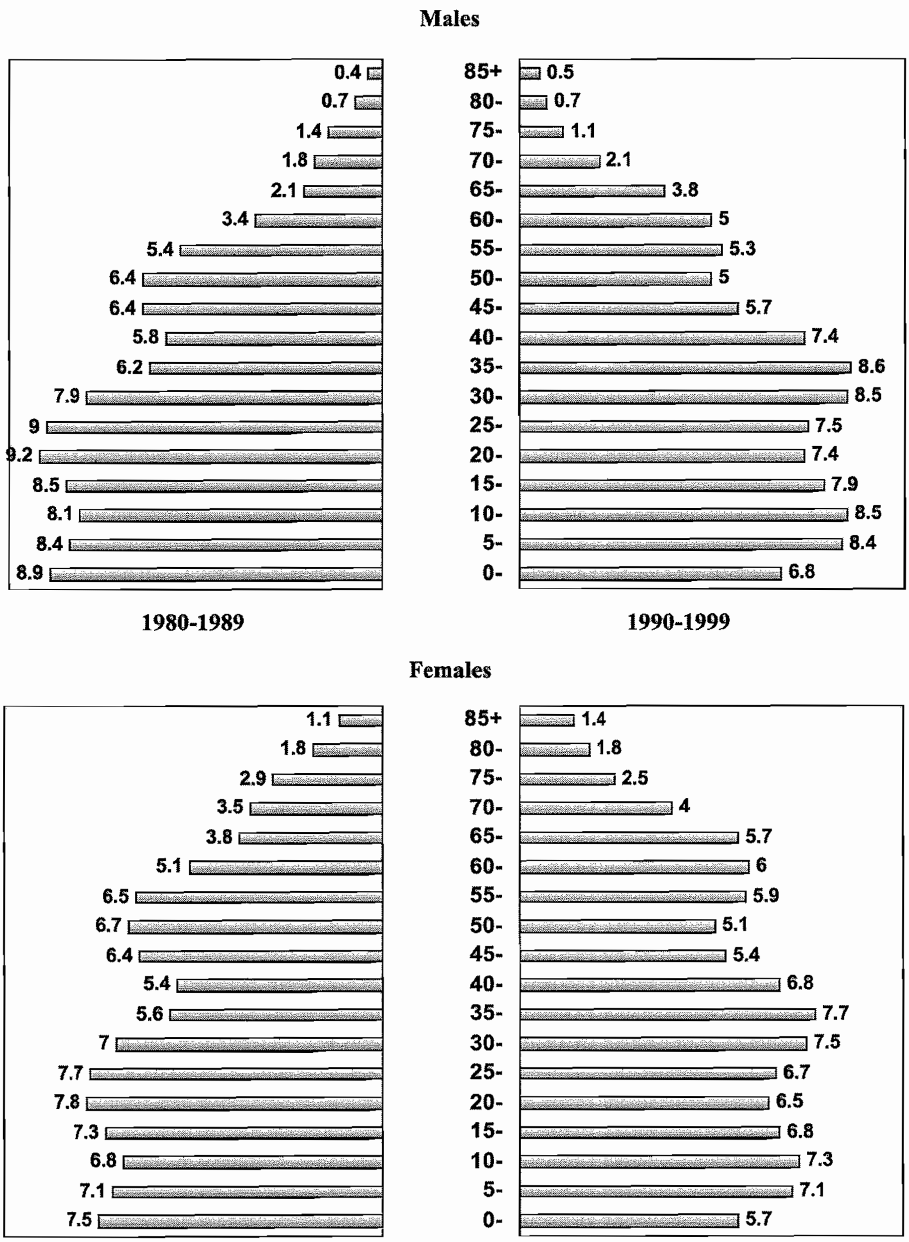

Fig. 1. Changes in population structure in Belarus (percentage).

frequencies of the leading types of cancer in Belarus, including thyroid cancer, which is not really leading (especially in males) but increased adversely within the last decade.

A considerable decrease in the proportion of stomach cancer (for males—20.6% in 1980–1989 vs. 14.5% in 1990–1999, for females—15.3% vs. 11.3%) correlates well with

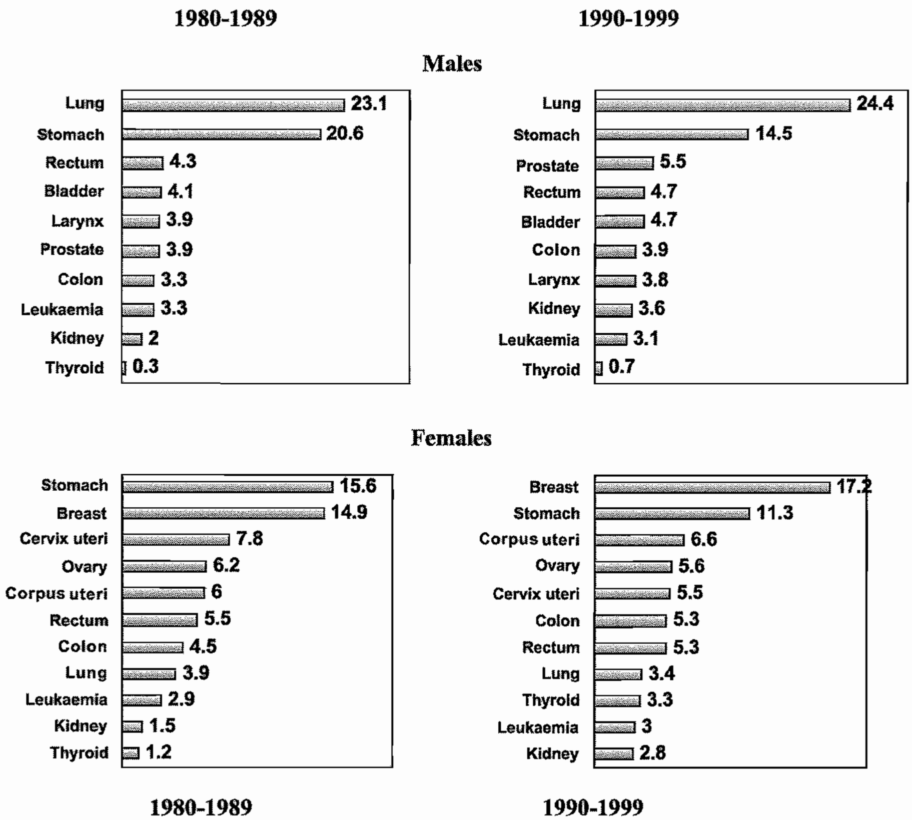

Fig. 2. Changes in the relative frequencies of the most common cancers in Belarus (non-melanoma cancer of the skin is not shown on the graphs).

the known (since early 1980s) tendency of this disease to decrease. A considerable increase in prostate cancer (3.9% vs. 5.5%), which moved from seventh to fourth position, should also be noted, as well as that in kidney cancer, whose proportion increased by 1.8 times.

Among female cancers, we would like to draw the readers' attention to the increase in the proportion of breast cancer (15.6% vs. 17.2%) which was previously ranked second place and, of course, to that of thyroid cancer, which considerably increased not just in children alone. Exchange of the positions between cancers of the cervix and corpus uteri should also be noted. The relative frequency of kidney cancer in males increased considerably (almost two times), though it moved to a lower position among other cancers.

3.3. Age-specific incidence rates

Age-specific incidence rates (ASIR) increased in their peaks (ages 65–80) on average in all cancers and in most of the leading sites except stomach and cervix cancers (Figs. 3

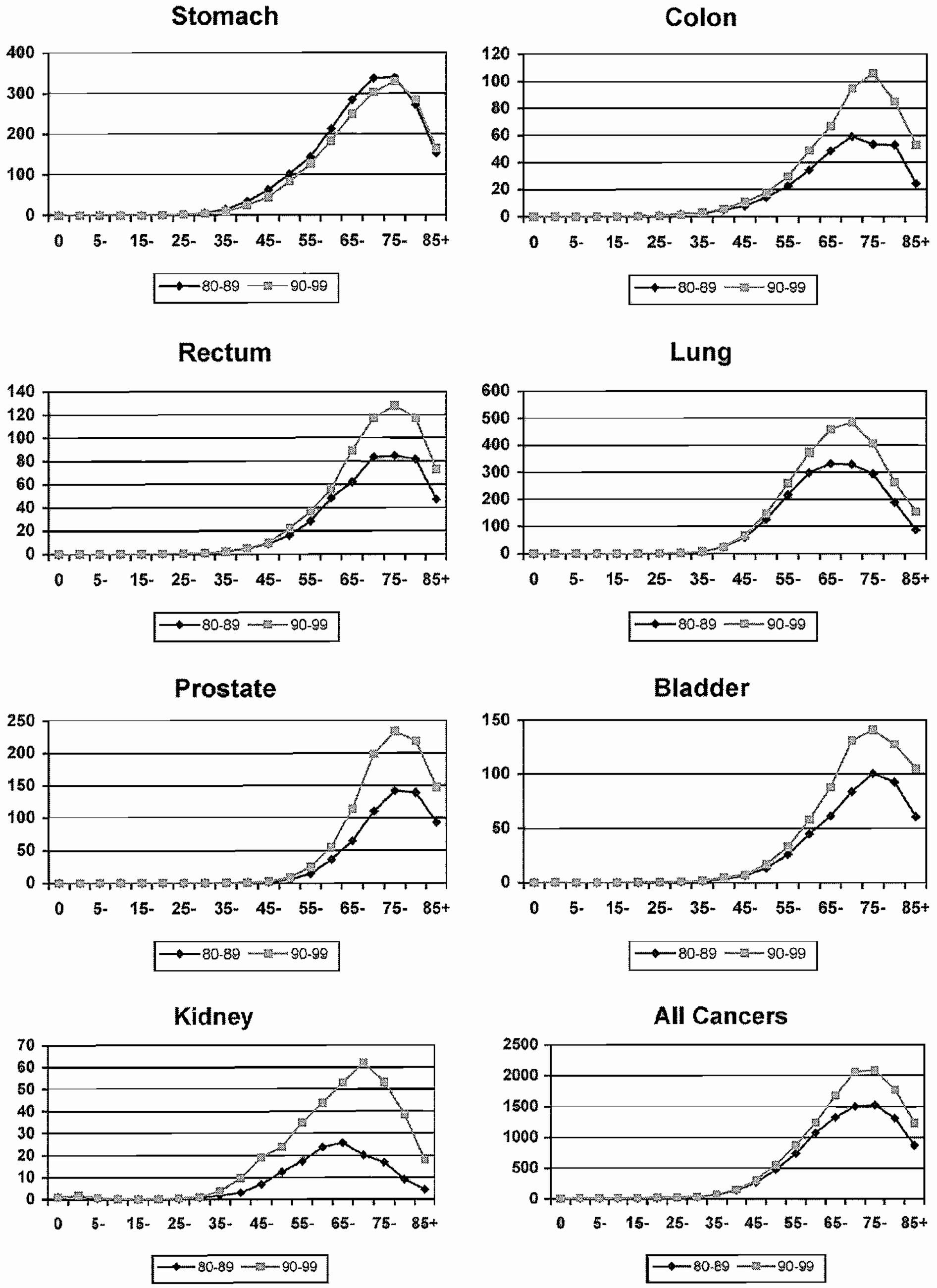

Fig. 3. Changes in age-specific rates of most common cancers in Belarus for the periods 1980–1989 and 1990–1999 (males).

and 4). Besides, while the nature of growth of ASIR for all cancers for males and females is about the same (1.3–1.4 times), in some sites, it has interesting features. The 5–10-year shift of peaks for the older ages is seen in colon and kidney for males and in rectum, breast, cervix uteri, kidney and leukemia for females.

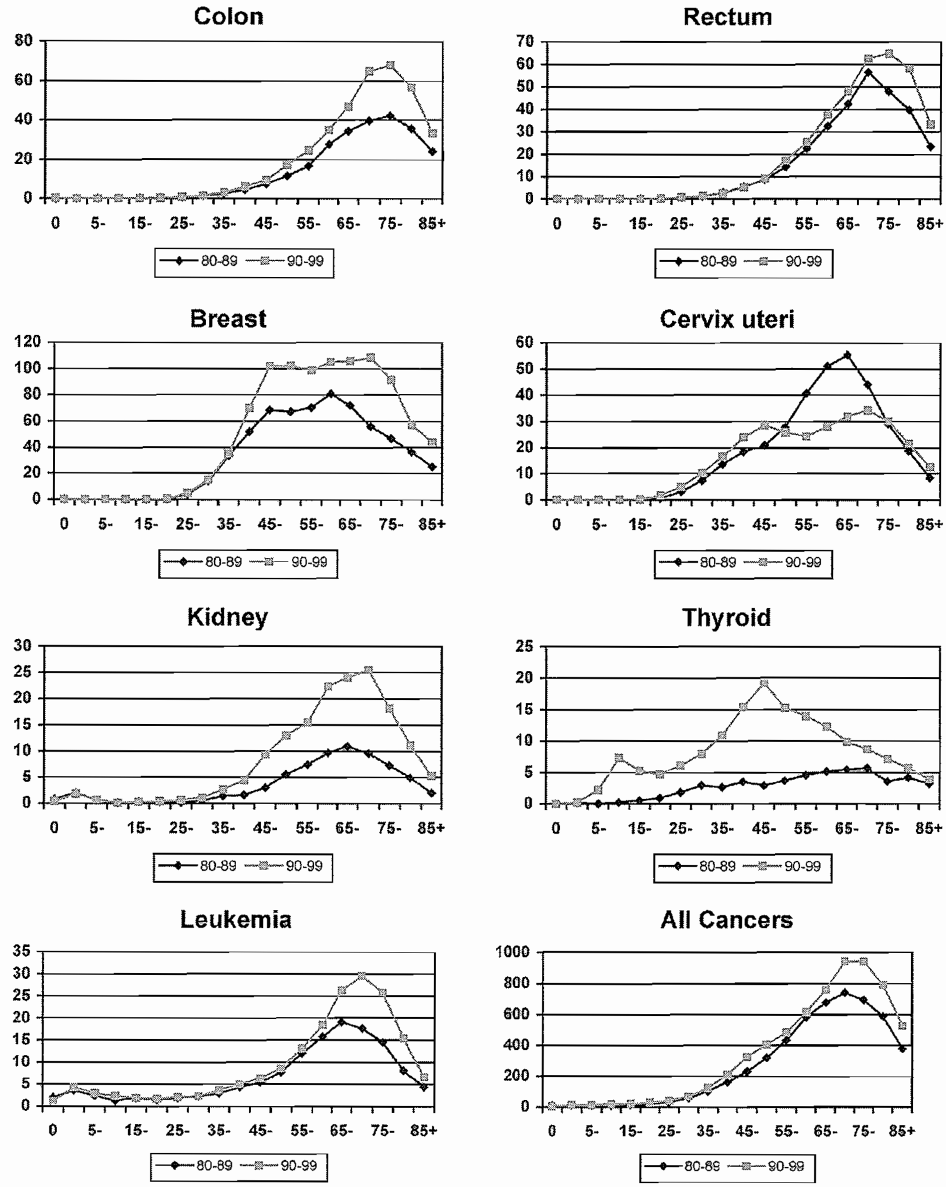

Fig. 4. Changes in age-specific rates of most common cancers in Belarus for the periods 1980–1989 and 1990–1999 (females).

While growth of peak ASIR for separate sites ranged normally from 1.4 to 2 times, growth of that for kidney cancer was three times and for ages 80–85, more than four times. It should also be noted that all age-specific incidence rates in kidney cancer for males starting from the age of 35 showed not less than twofold growth and, in age group 40–44, more than threefold.

For females, interesting peculiarities are seen in the changes of ASIR for breast cancer. Here, considerable growth of the rates started from the age of 35 and the peculiar "plateau" made up of the peak value of the ASIR in the ages from 45 to 74 can be seen.

It should also be noted that up to sevenfold growth of ASIR of thyroid cancer for females in the age group 45–49 was observed.

Completely untypical behavior of ASIR of cervix cancer was observed. It would be interesting to conduct a special study to explain this phenomenon.

As for males, a considerable increase in age-specific incidence rates of kidney cancer in age group of 65–74 was observed (more than 2.5 times).

3.4. Incidence

3.4.1. Common tendencies

On the average, in Belarus, crude rates of all cancers in total for males and females grew, as well as age-standardized rates (Fig. 5). However, while the average annual increase of crude rate was practically the same for the both study periods, the tempo of growth of the age-standardized rates in 1990–1999 was significantly lower for males than in 1980–1989 and remained practically stable for females (Table 1). At the same time, significant growth/fall of the average annual increase of crude rates correlates well with that of age-standardized rates for some of the separate sites.

3.4.2. Interregional variations

3.4.2.1. Belarus. In Belarus, time trend of all cancers in total showed an increase of ASR 1.24 times for males and 1.23 times for females, while the average annual increase in the

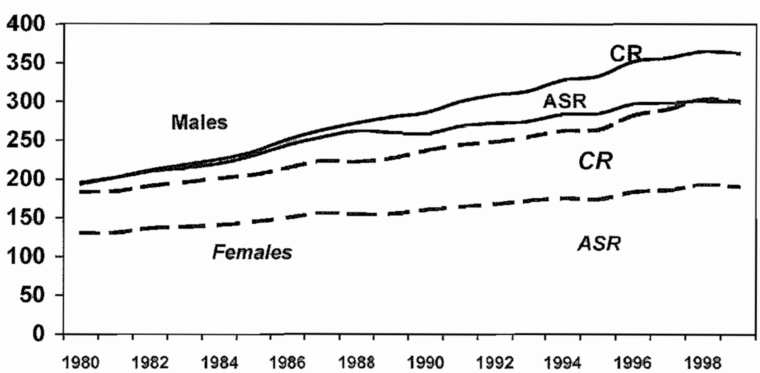

Fig. 5. Time trend in incidence (crude and age-standardized) rates for all cancers in Belarus (1980–1999).

Table 1

Average annual increase/decrease of the leading types of cancer in Belarus (periods 1980-1989 and 1990-1999)

Site	Crude rate				Age-standardized rate			
	SLR[a] (1980–1989)	95% CI	SLR (1990–1999)	95% CI	SLR (1980–1989)	95% CI	SLR (1990–1999)	95% CI
Males								
Stomach	−0.02	−0.29–0.25	−0.25	−0.42–−0.08	−0.36	−0.63–−0.1	−0.66	−0.8–−0.52
Colon	0.42	0.38–0.46	0.64[b]	0.57–0.72	0.38	0.32–0.44	0.39	0.32–0.46
Rectum	0.55	0.47–0.63	0.57	0.4–0.73	0.50	0.39–0.6	0.33	0.19–0.47
Pharynx	0.37	0.31–0.43	0.17[c]	0.04–0.3	0.28	0.21–0.35	0.07[c]	−0.04–0.18
Lung	3.41	3.09–3.73	1.56[c]	0.87–2.25	2.70	2.32–3.08	0.60[c]	0.07–1.13
Prostate	0.63	0.5–0.76	1.50[b]	1.36–1.64	0.64	0.53–0.76	1.00[b]	0.88–1.12
Bladder	0.59	0.44–0.73	0.65	0.57–0.73	0.52	0.38–0.67	0.38	0.3–0.46
Kidney	0.37	0.28–0.47	0.83[b]	0.76–0.9	0.31	0.22–0.41	0.62[b]	0.55–0.68
Thyroid	0.05	0.03–0.07	0.21[b]	0.16–0.27	0.05	0.03–0.07	0.18[b]	0.13–0.23
Leukemia	0.37	0.15–0.59	−0.08[b]	−0.28–0.11	0.29	0.09–0.49	−0.17[c]	−0.39–0.04
All cancers	9.89	9.2–10.59	9.14	8.07–10.21	7.98	7.11–8.84	4.79[c]	4–5.59
Females								
Stomach	−0.16	−0.37–0.04	−0.41	−0.55–−0.27	−0.24	−0.35–−0.14	−0.45	−0.49–−0.4
Colon	0.50	0.4–0.59	0.61	0.53–0.69	0.30	0.23–0.36	0.25	0.2–0.31
Rectum	0.39	0.28–0.5	0.24	0.13–0.35	0.20	0.11–0.3	0.07	0–0.14
Lung	0.31	0.17–0.46	−0.07[c]	−0.18–0.03	0.14	0.06–0.23	−0.10[c]	−0.16–−0.04
Breast	1.16	0.96–1.37	1.61	1.22–2.01	0.89	0.72–1.06	0.80	0.52–1.09
Cervix uteri	−0.24	−0.38–−0.11	−0.06	−0.2–0.07	−0.18	−0.29–−0.08	−0.09	−0.18–0
Corpus uteri	0.59	0.44–0.75	0.74	0.56–0.92	0.39	0.29–0.5	0.47	0.36–0.58
Ovary	0.28	0.17–0.39	0.15	0–0.3	0.20	0.1–0.29	0.07	−0.04–0.17
Kidney	0.24	0.2–0.29	0.49[b]	0.4–0.57	0.17	0.14–0.19	0.28[b]	0.22–0.34
Thyroid	0.15	0.09–0.2	0.95[b]	0.79–1.11	0.12	0.08–0.17	0.81[b]	0.64–0.98
Leukemia	0.29	0.1–0.47	0.01	−0.13–0.15	0.17	0.01–0.32	−0.03	−0.14–0.07
All cancers	5.30	4.75–5.84	7.75[b]	6.75–8.76	3.18	2.68–3.67	3.60	3.1–4.11

[a] SLR—average annual increase (slope of linear regression).

[b] Significant growth of the average annual increase.

[c] Significant fall of the average annual increase.

second decade was significantly lower than in the first one for males and practically stable for females (Tables 2 and 3). At the same time, there were some sites where there was indication that the average level was exceeded. For males and females, it was firstly the thyroid gland (SRR—3.32 and 4.07, accordingly). Then considerable growth of kidney cancer (SRR—2.22 and 2.2) and prostate cancer (SRR—1.7) should be noted.

3.4.2.2. Gomel region. Since the objective of this paper was to study the cancer incidence after the Chernobyl accident, the Gomel region drew special interest as the most radioactive contaminated area. Here, we pointed at those cancer sites, which significantly increased more than the average in Belarus. Presence of the Gomel data in Belarus data is not crucial, because they constitute far less than 30% of the total [1].

For males of the Gomel region, the following sites should be distinguished, in which growth significantly exceeds the Belarus average. Those are primarily urinary bladder (SRR—2.05 vs. 1.41) and prostate (2.16 vs. 1.7), as well as rectum (1.63 vs. 1.33) and lung (1.45 vs. 1.29). At the same time, it should be noted that incidence growth of prostate cancer did not significantly exceed that of Vitebsk region.

For females of the Gomel region, compared to data of Belarus, growth showed bladder cancer (SRR—2.34 vs. 1.44) and thyroid cancer (5.22 vs. 4.07) to be most affected. Also, the Gomel region significantly exceeded Belarus growth of age-standardized rate of lung cancer (1.3 vs. 1.02) and cancer of the corpus uteri (1.6 vs. 1.38).

3.4.2.3. Vitebsk region. For males of Vitebsk region, considerable growth of ASR in 1990–1999 should be noted for the cancers of thyroid (SRR—2.26), kidney (2.19), prostate (1.91) and colon (1.55) but it never significantly exceeded average growth in Belarus.

For females of Vitebsk region, considerable growth of thyroid cancer (SRR—3.58) and kidney cancer (2.14) should be noted, but it also did not significantly exceed average Belarus level.

3.4.2.4. Minsk region. Minsk region was weakly contaminated with radionuclides and had similar levels of cancer incidence with Gomel region in the pre-Chernobyl period.

In the Minsk region, first of all, significant excess of growth of ASR of leukemia for males (1.62 vs. 1.23), as well as for females (1.54 vs. 1.25), compared to entire Belarus should be noted.

In addition, for males of the Minsk region, considerable growth of ASR in 1990–1999 should be noted for the cancers of the thyroid (SRR—2.71), kidney (2.54), prostate (1.52) and colon (1.61), but it also did not significantly exceed average growth in Belarus.

Females of the Minsk region were leading those in Belarus in growth of breast cancer (SRR—1.56 vs. 1.42 in Belarus), but compared to Gomel and Vitebsk region, excess is not significant. As in other regions, incidence of thyroid cancer (SRR—3.64), kidney cancer (2.57) and colon cancer (1.46) considerably increased, but the growth was not significantly higher than the average in Belarus.

Table 2
Age-standardized rate ratio and average annual increase/decrease of age-standardized rate for the leading types of cancer in Belarus (periods 1980–1989 and 1990–1999; males)

Site	Region	ASR[a] (S.E.) 1980–1989	ASR (S.E.) 1990–1999	SRR[b]	95% CI (SRR)	SLR[c] (1980–1989)	95% CI	SLR (1980–1989)	95% CI
Colon	Belarus	7.68 (0.13)	11.08 (0.14)	1.44	1.38–1.5	0.38	0.32–0.44	0.39	0.32–0.46
	Vitebsk	6.92 (0.32)	10.71 (0.36)	1.55	1.39–1.73	0.42	0.23–0.61	0.33	0.09–0.57
	Gomel	6.26 (0.29)	10.4 (0.35)	1.66	1.49–1.85	0.25	0.12–0.38	0.46	0.28–0.63
	Minsk Reg	6.46 (0.29)	10.39 (0.34)	1.61	1.45–1.79	0.19	0.02–0.36	0.23	−0.05–0.51
Rectum	Belarus	9.93 (0.15)	13.21 (0.15)	1.33	1.28–1.38	0.50	0.39–0.6	0.33	0.19–0.47
	Vitebsk	10.4 (0.39)	13.62 (0.41)	1.31	1.19–1.44	0.72	0.35–1.1	0.55	0.32–0.78
	Gomel	8.06 (0.33)	13.14 (0.39)	1.63	1.48–1.79	0.19	−0.07–0.44	0.64	0.48–0.81
	Minsk Reg	9.23 (0.35)	12.12 (0.37)	1.31	1.2–1.44	0.60	0.38–0.82	0.24	−0.01–0.48
Lung	Belarus	53.32 (0.35)	68.67 (0.35)	1.29	1.27–1.31	2.70	2.32–3.08	0.60	0.07–1.13
	Vitebsk	57.98 (0.92)	73.35 (0.95)	1.27	1.22–1.32	3.12	2.08–4.16	0.36	−0.69–1.41
	Gomel	45.65 (0.79)	66.17 (0.87)	1.45	1.39–1.51	2.06	1.21–2.91	1.40	0.23–2.58
	Minsk Reg	56.2 (0.87)	78.01 (0.93)	1.39	1.34–1.44	3.26	2.63–3.9	1.57	0.68–2.47
Prostate	Belarus	9.15 (0.14)	15.59 (0.17)	1.70	1.64–1.77	0.64	0.53–0.76	1.00	0.88–1.12
	Vitebsk	9.03 (0.37)	17.27 (0.46)	1.91	1.75–2.09	0.92	0.58–1.25	1.59	1.17–2.01
	Gomel	7.16 (0.31)	15.5 (0.43)	2.16	1.97–2.38	0.40	0.26–0.53	1.33	0.78–1.88
	Minsk Reg	9.26 (0.35)	14.04 (0.39)	1.52	1.39–1.66	0.68	0.46–0.9	0.84	0.57–1.11
Bladder	Belarus	9.51 (0.15)	13.4 (0.16)	1.41	1.36–1.46	0.52	0.38–0.67	0.38	0.3–0.46
	Vitebsk	10.03 (0.39)	13.89 (0.41)	1.39	1.26–1.52	0.55	0.39–0.72	0.34	0.05–0.62
	Gomel	6.83 (0.31)	14.01 (0.4)	2.05	1.86–2.26	0.57	0.14–1.01	0.49	0.09–0.9
	Minsk Reg	9.56 (0.36)	13.1 (0.38)	1.37	1.25–1.5	0.82	0.53–1.11	0.31	0–0.62

Kidney	Belarus	4.69 (0.1)	10.42 (0.14)	2.22	2.12–2.33	0.31	0.22–0.41	0.62	0.55–0.68
	Vitebsk	4.71 (0.27)	10.31 (0.36)	2.19	1.94–2.48	0.20	−0.01–0.4	0.72	0.49–0.95
	Gomel	3.79 (0.23)	8.84 (0.33)	2.33	2.05–2.66	0.29	0.16–0.41	0.53	0.31–0.75
	Minsk Reg	3.94 (0.23)	10.03 (0.34)	2.54	2.25–2.88	0.46	0.25–0.67	0.59	0.3–0.88
Thyroid	Belarus	0.7 (0.04)	2.3 (0.07)	3.32	2.96–3.72	0.05	0.03–0.07	0.18	0.13–0.23
	Vitebsk	0.6 (0.09)	1.36 (0.14)	2.26	1.6–3.21	0.01	−0.05–0.06	0.08	−0.01–0.17
	Gomel	1.02 (0.12)	4.55 (0.25)	4.44	3.54–5.58	0.09	0.02–0.15	0.45	0.29–0.61
	Minsk Reg	0.69 (0.1)	1.88 (0.15)	2.71	2.01–3.66	0.07	0.01–0.13	0.01	−0.07–0.1
Leukemia	Belarus	7.67 (0.13)	9.45 (0.14)	1.23	1.18–1.29	0.29	0.09–0.49	−0.17	−0.39–0.04
	Vitebsk	7.63 (0.34)	8.72 (0.35)	1.14	1.02–1.28	−0.01	−0.24–0.23	−0.44	−0.73–−0.15
	Gomel	7.51 (0.32)	9.12 (0.34)	1.21	1.09–1.36	0.55	0.17–0.94	−0.10	−0.62–0.41
	Minsk Reg	6.08 (0.29)	9.85 (0.35)	1.62	1.44–1.82	0.18	−0.19–0.55	−0.14	−0.34–0.06
All Cancers	Belarus	230.24 (0.71)	285.57 (0.72)	1.24	1.23–1.25	7.98	7.11–8.84	4.79	4–5.59
	Vitebsk	233.95 (1.85)	287.95 (1.89)	1.23	1.21–1.26	7.79	6.11–9.47	4.50	1.81–7.19
	Gomel	213.31 (1.69)	293.11 (1.85)	1.37	1.35–1.4	7.19	4.75–9.62	9.00	6.91–11.09
	Minsk Reg	229.85 (1.74)	294.74 (1.82)	1.28	1.26–1.31	10.09	7.97–12.22	5.09	3.53–6.65

[a] ASR—age-standardized rate (world standard population).
[b] SRR—standardized rate ratio ($ASR^{1990-1999}/ASR^{1980-1989}$).
[c] SLR—slope of linear regression (average annual increase/decrease).

Table 3
Age-standardized rate ratio and average annual increase/decrease of age-standardized rate for the leading types of cancer in Belarus (periods 1980–1989 and 1990–1999; females)

Site	Region	ASR[a] (S.E.) 1980–1989	ASR (S.E.) 1990–1999	SRR[b]	95% CI (SRR)	SLR[c] (1980–1989)	95% CI	SLR (1980–1989)	95% CI
Colon	Belarus	5.97 (0.09)	8.45 (0.1)	1.42	1.36–1.47	0.30	0.23–0.36	0.25	0.2–0.31
	Vitebsk	5.54 (0.22)	8.57 (0.27)	1.55	1.4–1.71	0.29	0.14–0.44	0.24	0.07–0.4
	Gomel	4.97 (0.2)	7.35 (0.24)	1.48	1.34–1.64	0.36	0.21–0.5	0.34	0.23–0.46
	Minsk Reg	4.95 (0.2)	7.23 (0.24)	1.46	1.32–1.62	0.19	0.08–0.31	0.19	−0.01–0.39
Rectum	Belarus	7.27 (0.1)	8.37 (0.1)	1.15	1.11–1.19	0.20	0.11–0.3	0.07	0–0.14
	Vitebsk	7.46 (0.25)	8.7 (0.27)	1.17	1.07–1.28	−0.01	−0.11–0.09	−0.01	−0.24–0.23
	Gomel	6.47 (0.23)	7.88 (0.25)	1.22	1.11–1.34	0.19	0–0.37	0.18	0.07–0.28
	Minsk Reg	6.98 (0.24)	7.86 (0.24)	1.13	1.03–1.23	0.28	0.11–0.45	−0.03	−0.16–0.1
Breast	Belarus	23.87 (0.19)	33.91 (0.22)	1.42	1.39–1.45	0.89	0.72–1.06	0.80	0.52–1.09
	Vitebsk	24.09 (0.51)	33.61 (0.59)	1.40	1.32–1.47	0.78	0.47–1.09	0.46	0.2–0.72
	Gomel	22.84 (0.47)	33.58 (0.57)	1.47	1.4–1.55	0.72	0.2–1.24	0.78	0.06–1.51
	Minsk Reg	20.15 (0.45)	31.34 (0.55)	1.56	1.47–1.64	0.88	0.67–1.1	1.20	0.89–1.51
Cervix uteri	Belarus	11.97 (0.13)	10.85 (0.13)	0.91	0.88–0.94	−0.18	−0.29–−0.08	−0.09	−0.18–0
	Vitebsk	9 (0.3)	10.01 (0.32)	1.11	1.02–1.22	−0.18	−0.33–−0.02	0.17	−0.08–0.42
	Gomel	14.3 (0.36)	12.56 (0.36)	0.88	0.82–0.95	0.04	−0.16–0.25	−0.34	−0.65–−0.02
	Minsk Reg	11.06 (0.32)	12.83 (0.36)	1.16	1.07–1.26	−0.04	−0.29–0.21	−0.09	−0.52–0.35
Corpus uteri	Belarus	8.86 (0.11)	12.22 (0.13)	1.38	1.34–1.43	0.39	0.29–0.5	0.47	0.36–0.58
	Vitebsk	8.73 (0.28)	11.75 (0.33)	1.35	1.24–1.46	0.05	−0.18–0.27	0.46	0.24–0.69
	Gomel	8.14 (0.26)	13.04 (0.35)	1.60	1.47–1.74	0.32	0.08–0.55	0.78	0.49–1.06
	Minsk Reg	7.86 (0.26)	10.27 (0.3)	1.31	1.2–1.42	0.29	0.04–0.54	0.55	0.39–0.72

Bladder	Belarus	1.06 (0.04)	1.53 (0.04)	1.44	1.32–1.56	0.07	0.04–0.09	0.06	0.03–0.08
	Vitebsk	1.13 (0.09)	1.42 (0.1)	1.25	1.01–1.56	0.02	−0.03–0.08	0.04	−0.03–0.1
	Gomel	0.69 (0.07)	1.62 (0.11)	2.34	1.86–2.94	0.07	0.03–0.11	0.12	0.07–0.17
	Minsk Reg	1.13 (0.09)	1.46 (0.1)	1.28	1.04–1.58	0.08	0–0.16	0.07	−0.01–0.15
Kidney	Belarus	2.32 (0.06)	5.1 (0.09)	2.20	2.07–2.33	0.17	0.14–0.19	0.28	0.22–0.34
	Vitebsk	2.26 (0.16)	4.83 (0.22)	2.14	1.83–2.5	0.15	0.02–0.29	0.42	0.28–0.57
	Gomel	2 (0.14)	4.12 (0.2)	2.06	1.75–2.42	0.14	0.03–0.24	0.24	0.16–0.33
	Minsk Reg	1.96 (0.14)	5.05 (0.22)	2.57	2.2–3.01	0.25	0.13–0.37	0.18	0.02–0.34
Thyroid	Belarus	1.93 (0.06)	7.88 (0.12)	4.07	3.83–4.33	0.12	0.08–0.17	0.81	0.64–0.98
	Vitebsk	2.13 (0.16)	7.63 (0.3)	3.58	3.07–4.18	0.13	0–0.27	1.04	0.71–1.36
	Gomel	2.31 (0.15)	12.03 (0.39)	5.22	4.54–5.99	0.15	−0.03–0.33	1.09	0.68–1.51
	Minsk Reg	1.53 (0.13)	5.56 (0.25)	3.64	3.05–4.35	0.05	−0.03–0.13	0.47	0.28–0.67
Leukemia	Belarus	4.71 (0.09)	5.9 (0.1)	1.25	1.19–1.32	0.17	0.01–0.32	−0.03	−0.14–0.07
	Vitebsk	4.77 (0.23)	5.25 (0.24)	1.10	0.97–1.25	0.05	−0.04–0.14	−0.24	−0.49–0.01
	Gomel	4.44 (0.22)	5.89 (0.26)	1.32	1.17–1.51	0.31	0.06–0.56	−0.04	−0.34–0.26
	Minsk Reg	3.88 (0.2)	5.98 (0.24)	1.54	1.36–1.75	0.18	−0.06–0.43	−0.04	−0.3–0.22
All Cancers	Belarus	143.99 (0.46)	177.42 (0.5)	1.23	1.22–1.24	3.18	2.68–3.67	3.60	3.1–4.11
	Vitebsk	139.39 (1.16)	173.67 (1.28)	1.25	1.22–1.27	2.03	1.43–2.62	3.31	2.14–4.48
	Gomel	140.75 (1.11)	185.1 (1.3)	1.32	1.29–1.34	2.91	1.57–4.26	5.68	4.39–6.96
	Minsk Reg	129.93 (1.08)	166.33 (1.22)	1.28	1.25–1.31	2.86	2.01–3.71	3.33	1.37–5.29

[a] ASR—age-standardized rate (world standard population).
[b] SRR—standardized rate ratio ($ASR^{1990-1999}/ASR^{1980-1989}$).
[c] SLR—slope of linear regression (average annual increase/decrease).

4. Conclusions

In post-Chernobyl period, on the average in Belarus, moderate increase of the age-standardized cancer incidence rate was observed for males and females. While tempos of increase became lower practically for all leading types of cancer, rates increased considerably for cancers of the prostate, kidney, and thyroid gland for males, and for cancers of the kidney and thyroid gland for females. Average growth of incidence of all cancers in total significantly exceeded that in Belarus, not just in the Gomel region but also in the Minsk region. Very serious increases of kidney cancer for males and females and prostate cancer in all regions of Belarus, as well as bladder cancer in the Gomel region, require further investigations. Special attention should also be paid to the considerable increase of thyroid cancer in adolescents and adults (nearly sevenfold of incidence rate for females in the age group 45–49 was observed).

Reference

[1] P. Boyle, D.M. Parkin, Statistical methods for registries, in: O.M. Jensen, D.M. Parkin, R. MacLennan, C.S. Muir, R.G. Skeet (Eds.), Cancer Registration: Principals and Methods, IARC Scientific Publications, vol. 95, IARC, Lyon, 1991, pp. 126–158.

International Congress Series 1234 (2002) 267–279

Medical consequences of the Chernobyl Nuclear Power Plant accident: experience of 15-year studies

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Abstract

The results of the 15-year monitoring of health status among the different groups of victims of the Chernobyl disaster, i.e. clean-up workers, evacuated people, residents of contaminated areas and children, were overviewed. A significant increase in prevalence was noted among the clean-up workers for the diseases of the nervous system and sensitivity organs, endocrine system, blood circulation, digestion organs, urogenital system, blood and blood formation organs. The level of the disease exceeded the indices of morbidity among the adult population in Ukraine. A dramatic increase in the psychic disorders among this group was noticed especially in 1990–1993. It was determined during the cohort epidemiological studies that the most significant rates of growth of morbidity and the incidence of chronic non-tumoural diseases are observed among the clean-up workers of 1986–1987 compared with those who worked there during the subsequent years. Clean-up workers who suffered from acute radiation syndrome have high risks of realization of oncohematological pathology and combined immune deficiency. The results of monitoring the health status of the evacuated people showed the same negative tendencies. From 1988 to 1998, the ratio of healthy people decreased from 67.7% to 29.0%. The ratio of people with pathology increased from 31.5% to 71.0%. The increase of the morbidity level among the evacuees is conditioned mostly by the pathology of blood and blood formation organs, nervous system and sensitivity organs, endocrine system, organs of digestion, respiration, urogenital and osteomuscular systems. During the whole post-accident period, the condition of the medical and demographic indices of the population residing in radio-contaminated territories is worse than that in clean territories and in the country in general. In general, the stable demographic crisis was formed in radio-contaminated territories. Among the children's population that suffered as a result of the Chernobyl Nuclear Power Plant accident, the evacuees from the 30-km zone and the inhabitants of radiation-contaminated territories, including those relocated from the territories with a ground contamination density of 555–1480 kBq/m^2, the children born to clean-up workers and evacuees are the group of priority observation. All population health indexes have negative dynamics and are dramatically worse in comparison to the

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PII: S0531-5131(01)00616-1

same age of Ukrainian population. The incidence of all cancers in clean-up workers increased. Since 1995, all cancer incidence rates are higher in the population of Ukraine. The thyroid incidence rate in evacuees exceeds the national rate by five to six times. The priority tasks for the achievement of the goals of health protection for the people who suffered as a result of the Chernobyl catastrophe were determined.

Keywords: Chernobyl disaster; Health status; Long-term monitoring; Incidence; Prevalence

1. Introduction

Recognition of the consequences of the Chernobyl Nuclear Power Plant accident as a national catastrophe was reflected in the Ukrainian legislation. A concept of the Ukrainian national program for eliminating the consequences of the Chernobyl catastrophe and for the social protection of the citizens considers, as its main goal, the reduction of the total risk of health loss in the population of Ukraine and the reduction of social, psychological, ecological and economic effects of the accident [1].

The state social programs of our country, which are directed to the protection and rehabilitation of the health condition of those children and adults who suffered, confirm legislatively the Law of Ukraine "On Status and Social Protection of the Citizens who Suffered as a Result of the Chernobyl Catastrophe."

2. Health status of clean-up workers

A significant worsening health condition was detected among the clean-up workers of the Chernobyl Nuclear Power Plant accident during the post-accident period. The number of healthy individuals among this contingency that are young and relatively healthy at the time of their participation in the elimination of the consequences of the accident decreased from 78.7% to 10.3%, and to 7.2% among those who received whole-body external irradiation dose above 250 mSv as a consequence of the increase in mostly non-tumoural chronic diseases which are leading today in their morbidity, invalidism and mortality.

A significant increase in the number of patients among the clean-up workers was observed on the account of the diseases of the nervous system and sensitivity organs, endocrine system, blood circulation, digestion organs, urogenital system, blood and blood formation organs [2]. The level of the disease exceeds the indices of morbidity among the adult population in Ukraine (Table 1). A high frequency of psychic disorders was noticed especially in 1990–1993. Clinical observations of the condition of the nervous system in clean-up workers of 1986–1987 revealed symptoms of disruptions in the diencephalic-column fractions of the brain, dominating its depth and expression under the background of lesion of all the levels of the brain and its vascular system. The dynamics of the development of a disease in them is characterized by the progradient course of the pathological processes with the gradual deepening of neurological symptoms and the development of encephalopathy of different degrees of severity [3].

Table 1
The incidence of non-tumour diseases (per 1000 individuals) in the cohort of clean-up workers of 1986–1987 (the men are healthy at the time of participation in eliminating the consequences of the Chernobyl Nuclear Power Plant accident) and the healthy population of Ukraine (men and women) in 1988 and 1998

Class of diseases (ICD-9)	Clean-up workers		Adult population of Ukraine	
	1988	1998	1988	1998
All the diseases	209.0	2590.0	1018.6	1291.9
Infectious and parasitical diseases	2.5	11.0	29.4	36.9
Endocrine system diseases	0.9	172.9	27.0	40.3
Diseases of the blood and blood formation organs	0.1	7.9	1.7	6.5
Psychic disorders	3.1	41.4	49.2	49.5
Diseases of the nervous system and sensitivity organs	14.0	522.3	106.4	144.9
Blood circulation system diseases	5.2	584.8	158.7	349.4
Respiratory organ diseases	118.5	303.3	286.5	230.8
Diseases of the digestion organs	7.4	601.5	86.2	126.9
Diseases of the urogenital system	1.6	66.7	52.3	76.6
Diseases of the skin and subcutaneous fat	7.6	17.5	38.0	43.1
Diseases of the osteomuscular system	18.8	241.6	64.1	84.8

Diseases of the digestion organs, blood circulation system, nervous system and sensitivity organs were of the first rank in the structure of the diseases first revealed. These three classes of diseases include 85–87% of the causes of invalidism, and diseases of the blood circulation system rank first among the causes of death among the clean-up workers. During the last years, the diseases of digestion organs are the most common. Their structure pathology of the hepatobiliary system is 42–46%. During the first 5 years after the accident, among the diseases of the nervous system and sensitivity organs, a significant contribution was made by vegetovascular disruptions, and further, by encephalopathies, myelopathies, polyneuropathies and eye diseases. In the structure of the diseases of the blood circulation system, the contribution of essential hypertension is 39–41%, ischemic heart disease, −20%, and cerebrovascular pathology, −15%. The bulk of the diseases of the endocrine system is thyroid pathology (73–78%). The contribution of chronic non-specific diseases of the bronchi and lungs is growing in the structure of the diseases of the respiratory organs.

It was determined during the cohort epidemiological studies that the most significant rates of the growth of morbidity and the incidence of chronic non-tumoural diseases are observed among the clean-up workers of 1986–1987 compared with those who worked there during the subsequent years.

The 14-year observation of the health condition of clean-up workers who suffered from acute radiation syndrome testifies on the high risk of the realization of oncohematological pathology and combined immune deficiency. Skin lesions have recidivate among 1/3 of the patients. Radiation cataracts, laboratory hypothyrosis and the organic pathology of the nervous system dominate the clinical symptoms. More than 90% of the reconvalescents of acute radiation syndrome are invalids of two groups. The basic cause of death is instant heart death.

The efficiency of the countermeasures on the prophylaxis of the stochastic effects of irradiation in the group of reconvalescents of acute radiation syndrome is considered as extremely problematic and doubtful, and non-stochastic ones are more probable under the condition of regular supportive therapy at the hospital, ambulance and health center and resort stages and the elimination of other common risk factors which depend, first of all, on the personal position of the victims [4].

The obtained data testify on the appropriate dependence of the formation of chronic non-tumour morbidity among clean-up workers from irradiation dose. At different periods after their participation in the elimination of the Chernobyl Nuclear Power Plant consequences, the risk of the development of some diseases of the blood circulation system, digestion organs, nervous system, thyroid and urogenital system was higher among the clean-up workers who received an irradiation dose above 250 mSv.

The annual decrease in mortality was observed among the clean-up workers. Indices of mortality approached the mortality level among the whole Ukrainian population of working capability age. During the last 6 years, the average annual rates of the increase of mortality from diseases of the organs of blood circulation, respiration, digestion and endocrine pathology grew two times. Nowadays, diseases of the blood circulation system rank first in the mortality cause structure.

3. Health status of evacuees

According to the Ukrainian State Registry of the Individuals who Suffered as a Result of the Chernobyl Catastrophe, among the adult population evacuated from the city of Pripyat’ and the 30-km zone around the Chernobyl Nuclear Power Plant, negative tendencies of changes in health condition were noticed. From 1988 to 1998, the ratio of healthy people decreased from 67.7% to 29.0%, whereas the ratio of people with pathology increased from 31.5% to 71.0%. For the above-mentioned period, the incidence of diseases increased three times, and primary morbidity increased two times on the account of more significant excess of diseases compared with the Ukrainian adult population. The increase in the morbidity level among the evacuees is conditioned mostly by the pathology of blood and blood formation organs, nervous system and sensitivity organs, endocrine system, organs of digestion, respiration, urogenital and osteomuscular systems. Indices of such classes of diseases of the nervous system, blood and blood formation organs, psychic disorders, nervous system and sensitivity organs, systems of blood circulation, digestion and osteomuscular system exceed the population level.

The level of primary morbidity of the thyroid increased by more than 1.5 times among the evacuees, mostly on the account of acquired hypothyrosis, thyroiditis and non-toxic nodular goiter. The annual level of thyroid disease is higher in women than in men. The frequency of the diseases increases with age. Its increase is more pronounced from the age of 30 [5].

Appropriate peculiarities are noticed in the disease structure among the evacuees. During the first post-accident years, the leading role was played by psychic disorders and their contribution in the structure reached to 14%. During the subsequent years, diseases of the organs of blood circulation, respiration, nervous system and sensitivity organs and digestion organs were more common. It is necessary to point out the considerable increase in the dynamics of the structure in the contribution of the diseases of the digestion organs, which rank first in the disease incidence structure after ranking third, and that in the structure of the primary diseases ranks second.

Special cohort studies of the morbidity of evacuees with different terms of evacuation from Pripyat' and the 30-km zone around the Chernobyl Nuclear Power Plant (during the first 2 days and also 8–12 and 19–50 days after the catastrophe) established that the highest morbidity level was among the evacuees from Pripyat', e.g. evacuees of earlier terms. Here, the morbidity accumulated for the period of 1988–1998 in the cohort of evacuees of the first 2 days after the catastrophe was 7780.7±212.4‰. The lowest indices were detected in the cohort of individuals evacuated at later terms (19–50 days). Here, the index of the accumulated morbidity was two times lower (3124±108.8‰). Among the evacuees of 8–12 days, the morbidity index was 5437.6±62.2‰. Appropriate differences among the evacuees of different terms are also observed as for the levels of the diseases by classes and nosological forms and structure of the diseases—it is connected with both the factor of age and the impact of complex factors of the accident (stress, value of dose loading, etc.).

During the study of mortality dynamics among the evacuees for the above-mentioned period, it was established that for a given period, the total mortality level did not exceed that of the population. Meanwhile, the study of age changes revealed that at separate years (1993 and 1994), the mortality level among the adolescents (age: 15–17) was higher than that of individuals aged 18–29 or in concordance with the mortality level in elderly age groups. In the structure of the causes of death, the diseases of blood circulation organs (47.6–83.1%), neoplasms (7.4–16.5%) and traumas and intoxications (2.7–19%) have the highest proportion [6].

Considerable changes in health condition were registered also among the population residing in radiation-contaminated territories. For the period of 1988–1998, the incidence of the diseases and primary morbidity grew by more than two times (respectively, from 620.9‰ to 1275.6‰ and from 309.5‰ to 746.0‰). The growth of morbidity is registered almost in all the classes of diseases, especially in the class of diseases of blood and blood formation organs (10.8–15.4 times), endocrine pathology (4.1–8.1 times), nervous system and sensitivity organs (3.8–5.0 times) and skin and subcutaneous fat (4.0–4.6 times). The level of morbidity of the organs of digestion, urogenital and osteomuscular systems increased by more than two times. From 1993 to 1994, the indices of morbidity among the victims exceed that of the population on the account of rather higher annual rate of excess of indices among the population of radio-contaminated areas.

The morbidity among the inhabitants of radio-contaminated territories depends on the zone of residence. In the period of 1988–1997, the highest excess was registered in zone 2 (surface deposition of ^{137}Cs is exceeding 15 Ci/km^2). In zone 3 (surface deposition of ^{137}Cs is 5–15 Ci/km^2), the level of morbidity increased by 2.3 times, while in zone 4 (surface deposition of ^{137}Cs is 1–5 Ci/km^2), 1.4 times. The average annual rate of excess of morbidity indices in zone 2 compared with zone 3 is higher by 2.9 times, while with zone 4, 5.6 times. For the first time, a higher level of revealed pathology was reliably established in zone 2 only compared with the population level. Such differences in the morbidity indices among the inhabitants of different zones are registered almost in all the classes of diseases. It should be pointed out however that in zones 3 and 4, like in zone 2, very high levels of psychic disorders were registered in separate years, reaching 11–16‰ in zone 3 and 10.6‰ in zone 4. In zone 2, the maximum level of this index reached to 69.7‰ compared with 4.4–5.4‰ among the adult population.

During the special cohort study of the inhabitants of radiation-contaminated territories, the reliable dependence of the formation of some classes and forms of diseases from thyroid irradiation dose was established. In individuals with thyroid doses exceeding 200 cGy, the high relative risk of the development of diseases of organs of blood circulation, especially cerebrovascular pathology, was noticed compared with those for whom this dose is below 30 cGy. The risk of the formation of endocrine pathology and diseases of the osteomuscular system is also reliably higher [7].

Molecular and genetic studies conducted in the Urology and Nephrology Institute, Academy of Medical Sciences of Ukraine, in collaboration with the specialists of the Medical Center of Osaka University (Japan), testify that the mutation inactivation of the *p*53 tumour-suppressor gene takes place in 53% of the cases, and in 96% of the cases—the development of precancer changes in the urothelium of the urinary bladder among the patients with prostate adenoma—of the inhabitants of territories contaminated with radionuclides as a result of long-time chronic impact of low ionizing irradiation doses (more than 14 years). It leads to genetic instability with the possible development of mostly invasive forms of urinary bladder cancer.

4. Demographic features

Beginning from 1990 to 1991, the symptoms of demographic crisis were observed in the country. Its peculiarities are the considerable decay of birthrate and rapid growth of mortality among the population. Infant mortality remains on the increased levels. Population morbidity, especially among children, is constantly growing. Everything takes place under the negative radiation and ecological conditions caused by the Chernobyl catastrophe and its consequences. The collective population irradiation dose is growing because more than 2.5 million people reside in the localities with increased levels of radioactive contamination, and for 15 years, they have been experiencing the impact of chronic irradiation by low radiation doses.

During the whole post-accident period, the condition of the medical and demographic indices among the population residing on radiation-contaminated territories is worse than on non-contaminated territories and in the country in general [8]. It was reflected more essentially on the levels of basic indices, characterizing the dynamics of population number, its structural peculiarities and processes of renovation. The dynamics of the formation of demographic indices on radiation-contaminated territories has such peculiarities. For the first 2 years after the accident, the local decay of birthrate and the increase of infant mortality were registered. At the third to fifth years, the return of indices to pre-accident levels took place. From the sixth year, the decrease of birthrate, increase of infant mortality, total mortality and mortality from separate causes of death and the decrease of life span were registered. In general, stable demographic crisis took place on radiation-contaminated territories. Its consequences will negatively influence the health condition of future generations in those areas.

With such integral index as a human development index, the health condition of the inhabitants in the areas that mostly suffered from the catastrophe is worse than in the country in general (Fig. 1). The human life index is an integral index where the methodology of calculation is based on four indices—life span, gross internal product per capita, education level and number of citizens who are studying.

The lowest levels of this index were observed on radiation-contaminated territories. Of special concern is the decrease of the average expected life span (AELS). For the whole post-accident period, the AELS for the individuals of both sexes on radiation-contaminated territories in the Zhitomir, Kiev and Chernihiv regions decreased within 4–5 years, while that in the control Poltava region and in Ukraine in general decreased within 3 years.

Studies of the past years showed that external causes of death (incidents, traumas and intoxications), neoplasms and somatic diseases are the leading ones in the reduction of life span of the population both in radio-contaminated and non-contaminated territories. The average expected life span under the mortality from somatic pathology is essentially higher (12–16 years for men and 4–7 years for women) than in the case of oncological diseases irrespective of the territory studied. Analysis of age-relative risks by causes of death revealed that the decrease of AELS among the population is conditioned, first of all, by the mortality among the individuals of both sexes of working capability age from somatic pathologies and—presumably for men—from external causes. Under the general tendency of the growth of risks of death from neoplasms of individuals aged 45 and above both in radio-contaminated areas and in the control, the presence of groups of increased risk was observed for this pathology. Thus, in the Zhitomir region, these are children of ages 1 and above and women of ages 20–29, and in the Kiev and Chernihiv regions, individuals of both sexes of ages 15–29.

For the whole period of observations, the reliable growth ($p<0.001$) of mortality from neoplasms was revealed in the most radio-contaminated areas and in Ukraine in general. Here, the average annual rates deviated within 0.015–0.04 per 100 000 people. During the post-accident period, the average annual rates of excess were significantly higher in the Kiev, Zhitomir and Chernigiv regions than in the control region of Poltava

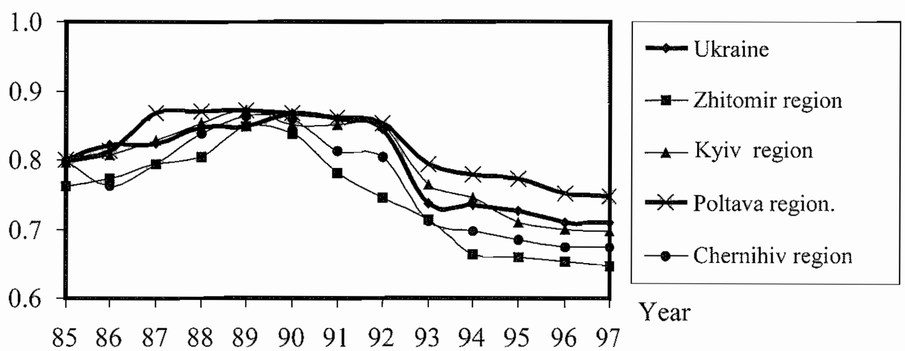

Fig. 1. Dynamics of the human development index in the most radio-contaminated areas in 1985–1997.

and Ukraine in general (by two times). The highest rates of excess were revealed in the Ivankiv district of the Kiev region and in the Luginy and Narodichi districts of the Zhitomir region.

Consequences of 15-year studies after the Chernobyl catastrophe still do not give the opportunity to determine the size of the contribution of ionizing irradiation into the worsening demographic indices, including the mortality from diseases which could be induced by irradiation. The data obtained testify on the changes of basic demographic indices during the post-accident period, and the prognosis calculations testify on the subsequent worsening of the medical and demographic situation in radio-contaminated territories.

5. Production and health status of children

Among the pregnant women residing in areas with increased level of radiation contamination, a considerable decrease in birthrate takes place (from 30% to 40%). The growth of somatic morbidity (cardiovascular pathology — 2 times, diseases of the kidney — 3 times, thyroid diseases — 5 times and anemia — 10 times compared with the pre-accident period) is taking place under such background.

The presence of the connection is proven between the accumulation of separate radionuclides in the placenta and fetus body weight. Here, the decrease in the body weight (hypotrophy) of a neonate takes place. It takes place three times more often than in the total population.

The condition of reproductive health of women from radiation control areas is determined clinically by the increase of the frequency of chronic inflammatory diseases of the genitals, hyperplastic processes (1.5–2 times) and the decrease of fertility by almost 1.5 times. Disruptions of the hormonal function of the fetoplacentary complex and the thyroid gland are established, which lead to the appearance of the complicated course of pregnancy and labors, worsening of the condition of a fetus and its intrauterine death as a result of hypotrophy, hypoxia and developmental malformations under the background of characteristic changes. The health quality of the neonates is decreasing, while neonatal losses and invalidism in children are growing.

Based on the immunological monitoring of women and children's population that suffered, regularities are revealed in the changes of the immune status in a "pregnant woman–fetus-child" biological system. The concept is suggested for the disruptions of immunity in children from radiation control areas, which assumes that the development of immunodeficiency conditions and autoimmune pathology at the above-mentioned contingency of children begins from the activation of separate links of intrauterine fetus with their subsequent exhaustion and disruptions of endocrine regulation of immune homeostasis at children, first of all, on the account of the changes in the hypophysis–thyroid system.

In concordance with the data of the first post-accident years, the number of healthy evacuated children and born to clean-up workers decreased from 30% to 2.8–5% in different observation groups, and the percentage of the children increased by more than two times whose health condition belong to the third health condition group (62%). The number of children-invalids among the survivors exceeds four times the average population level in Ukraine.

An increase in the level of somatic diseases was revealed and registered during medical follow up [9]. Thus, in 1987–1988, this index was 25 948, and in 1999, it increased by almost two times to 49 967. The most pronounced changes consider the index of the morbidity of digestion organs (4659 in 1998; 10 122 in 1999) and the nervous system (2369 and 4350, respectively). Comparison with children of the same age testifies on the considerable difference between the levels of this index (by the data of 1999 which is three times higher among the children who suffered). Clear tendency is determined as for the increase of risk of the development of pathology of digestion organs, nervous system and diseases where the main chains in the pathology are the changes of immune condition (allergic bronchitis, dermatitis and colitis) compared with the children of the same age.

The structure of all diseases among the children's population that suffered acquired qualitative changes: ranking first is the diseases of digestion organs (chronic diseases of the liver, gallbladder, biliary ways and pancreas, gastritis and gastroduodenitis). It is different from the general regularities of the formation of morbidity in the populations of children's age (respiratory organ diseases are in the first rank in the structure of all the diseases in children's populations). The age of first diagnosis of the diseases of digestion organs is lowered among the children's population that suffered. More often, diseases of the liver, gallbladder, biliary ways and pancreas, gastritis and gastroduodenitis are diagnosed for first time in a younger school age.

The growth of the level of neurotic conditions is revealed among the children born to clean-up workers. The structure of this nosological group is mostly represented by anxiety neurosis. The frequency of logopedic pathology exceeds by almost two times the similar index in the control registry.

It was determined that the basic risk of health loss for children's population residing on radio-contaminated territories is connected with the diseases of blood and blood formation organs, endocrine system, digestion organs and psychic disorders. For the evacuees from the 30-km zone, these are psychic disorders and diseases of the digestion organs and nervous system. Without the impact of the consequences of the Chernobyl Nuclear Power Plant accident, it would be possible to avoid the diseases of the endocrine system by 24%, diseases of blood and blood formation organs by 33%, psychic disorders by 52% and digestion organ diseases by 24%.

The formation of morbidity is connected with the impact of both radiation and non-radiation factors (ground contamination with radionuclides, heavy metals, pesticides, chemical composition of potable water, etc.) Part of the ionizing irradiation is from 2% to 20%.

Among the children's population that suffered as a result of the Chernobyl Nuclear Power Plant accident, the evacuees from the 30-km zone and those residing in radiation-contaminated territories including those who were relocated from the territories with a contamination density of 555–1480 kBq/m^2, and children born to clean-up workers and evacuees are the priority observation group.

An increase in the general population morbidity (from 455.4 in 1987 to 1519.6 in 1999) and morbidity by all the basic disease classes, the decrease of the ratio of practically healthy children (from 27.5% in 1986–1987 to 8.3% in 2000) and an increase in the number of children with chronic diseases (from 8.4% in 1986–1987 to 55.5% in 2000) and children-invalids are established on the population level. The most unfavourable changes were observed among children with high thyroid irradiation doses (above 200.0 cGy) and children irradiated in the uterus. Part of the practically healthy children among them does not exceed 2.6–5.0%.

Beginning from 1986, the determined effects of thyroid irradiation were observed: the primary functional response was detected in 1986–1987, while the beginning of the formation of chronic autoimmune thyroiditis was detected in 1990–1992, and the clinical realization of the diseases was observed in 1992–1993. In 1993–1995, in the group of evacuees from the 30-km zone, non-tumoural diseases of the thyroid (chronic thyroiditis and hypothyrosis) were 0.057–0.089 per 10 000 children, while those among the children residing on contaminated territories were 0.083–0.160 per 10 000, respectively. In 1998, the incidence of chronic thyroiditis and hypothyrosis was 320 per 10 000 children, while those among inhabitants of territories of radioecological control was 145, respectively.

Excess of thyroid cancer incidence among children and adolescents in Ukraine is confirmed by the dynamics of the disease. During the pre-Chernobyl period in 1981–1985 in Ukraine, the level of thyroid cancer incidence among the children of ages 15 and below was 0.05 cases per 100 000 children. Nowadays, there are 1400 verified cases of thyroid cancer among the children in Ukraine. Its significant growth is determined beginning from 1990. In 1986–1990, the thyroid cancer incidence among the children's population in Ukraine was 0.11 per 100 000, in 1991–1995, 0.41 per 100 000 and in 1996–2000, about 0.40, e.g. in the last decade, it was eight times higher.

The presence of mutations in the genome of children born to families of parent-clean-up workers and the structural–functional condition of the bone tissue of the children born to mothers irradiated at the children's age were determined. A tendency of the increase of the mutation levels by 1.5 times is detected only for the children conceived when their parents were exposed to the ionizing irradiation during their work at the Chernobyl Nuclear Power Plant. This fact testifies that the male genital cells could be sensitive to the mutagenic impact of ionizing irradiation only on the stage of meiosis (spermatogenesis).

At delayed terms of the post-accident period, the prognosis of the children's health remains unfavourable. A high number of children is preserved in groups of the risk of the development of pathologies of the most irradiated organs and systems: thyroid, 32.6% (in control — 15.4%, $p<0.05$); respiratory organs, 26.0% (in control — 13.7%, $p<0.05$); cardiovascular system (taking into account vegetovascular dystonia), 57.8% (in control — 31.8%, $p<0.05$); gastrointestinal tract, 18.9% (in control — 8.9%, $p<0.05$); immunological insufficiency, 43.5% (in control — 28.0%, $p<0.05$); and endocrine infertility in girls, 32.0% (in control — 10.5%, $p<0.05$).

In children born to mothers irradiated in the children's age of the disruption of calcium–phosphorus metabolism, the metabolism of the bone tissue (decrease of activity of osteoblasts) is revealed already in early infancy. In the future, it could lead to the development of structural–functional disruptions in the bone tissue. Earlier, structural disruptions in the bone tissue were revealed in girls (by the data of ultrasound densitometry).

The chronic radiation affliction of children born to clean-up workers and inhabitants of radiation-contaminated territories leads, first of all, to the disruption of the integrative function of the central nervous system in the outlook of the regional changes of vegetative innervation, vascular dysfunction of different degrees of expression and multiple disruptions of higher nervous activity. Under the background of these disruptions, the development of encephalopathies is characterized by the most severe course such as those individuals who were exposed to ionizing irradiation at the children's age.

Mortality among the children who suffered during the whole post-accident period is lower or on the level of the total index of children's mortality, ages 0–14, in Ukraine.

6. Cancer mortality and morbidity

A long-term monitoring of malignant neoplasm diseases among the clean-up workers of the Chernobyl Nuclear Power Plant, accident evacuees and the population residing in radiation-contaminated territories showed the difference of these processes compared with the total Ukrainian population.

Malignant neoplasm morbidity among the clean-up workers shown by the data of 1990–1998 grows constantly, and beginning from 1995, exceeds similar indices for the appropriate age group of the Ukrainian population. Thus, in 1998, malignant neoplasm morbidity among the clean-up workers was 650.0 per 100 000 and in appropriate age groups of the Ukrainian population, 540.0 per 100 000. Breast cancer incidence in women-clean-up workers (1990–1998) and among the population residing in territories contaminated with radionuclides (1993–1997) increased by 1.5 times. It is a common knowledge that radiogenic solid tumours could also appear within 30–50 years after irradiation, that is why there is a necessity of subsequent monitoring of malignant neoplasm diseases among the clean-up workers, evacuees and the population of territories contaminated with radionuclides for timely detection of possible stochastic effects of irradiation. Thyroid cancer morbidity among the clean-up workers of 1986–1987 exceeds four to five times the indices for the appropriate population age groups (SIR: 415.4%, 95% CI: 304.6–529.2%). It testifies on its connection to irradiation.

The total morbidity level among the evacuees as for the malignant neoplasms during 1990–1998 does not essentially differ from the morbidity level of the Ukrainian population, and in 1998, it was 256.3 per 100 000. However, thyroid cancer morbidity exceeds five times this index among the appropriate age groups of the Ukrainian population [10].

During the period of the study (1980–1998) among the population residing in contaminated territories, the level of malignant neoplasm morbidity is constantly growing.

7. Concluding remarks

The results of the 15-year observation of the health condition of the population categories that suffered from the Chernobyl Nuclear Power Plant accident factors testify that despite of the unprecedented scale of the accident, the medical service, thanks mostly to the efforts of the Ukrainian medical workers, managed to provide, in general, the necessary amount of measures and actions directed on the protection of the population that suffered against the impact of the negative factors of the accident in the limits allowed by the possibilities of that time.

During the whole post-accident period, the condition of the medical and demographic indices of the population residing in radio-contaminated territories is worse than that on clean territories and in the country in general. In general, stable demographic crisis was formed in radio-contaminated territories. Its consequences will negatively influence the health condition of future generations.

For subsequently 10 years (until 2010), it is necessary to expect the preservation of the tendency for the growth of morbidity of the same classes of diseases, and possibly, malignant neoplasms by taking into account the natural aging of the contingencies that suffered.

The morbidity by many classes of diseases among the survivors of all the categories is constantly growing during the post-accident years. Thyroid and breast cancer incidence reliably increased among the oncological pathologies.

Comparison of health indices of the survivors with appropriate indices of the population that did not suffer from the Chernobyl Nuclear Power Plant accident testifies that the worsening of both the health condition of the population that suffered and the general health condition of the Ukrainian population takes place under the influence of negative factors that are different in their nature and not only under the impact of ionizing radiation.

Among the children's population that suffered as a result of the Chernobyl Nuclear Power Plant accident, the evacuees from the 30-km zone and inhabitants of radiation-contaminated territories, including those relocated from the territories with ground contamination density of 555–1480 kBq/m^2 and children born to clean-up workers and evacuees are the group of priority observation.

The determination of population health condition and the implementation of the measures on its protection for the survivors are among the most important problems in the system of measures on the elimination of the consequences of the Chernobyl catastrophe. Basic efforts should be directed on the achievement of the level of basic health indices in all the categories of survivors that are not worse than the same indices for the appropriate groups of population in clean territories.

An increase in the efficiency of the measures as for the minimization of medical consequences of a radiation accident, taking into account the experience acquired on the engagement of efforts of health care establishments, is possible only under the condition of existence of timely planning of organizational, medical and sanitarian, social measures and implementation of the population protection system into practice. Their implementation should take place in concordance with the Draft National Program for the Minimization of the Consequences of the Chernobyl Catastrophe for 2001–2005 and until 2010.

Priority tasks for the achievement of the goals of health protection for people that suffered as a result of the Chernobyl catastrophe should provide first of all:

- the provision of highly qualified and guaranteed medical aid to individuals included into the priority groups of medical care and patients with realized pathology;
- the development and implementation of scientifically substantiated efficient methods of therapy of radiogenically induced and other invalidizing diseases for survivors at a delayed period;

- the development and implementation of prophylactic measures on the diminishing morbidity level and health protection for children and adults;
- the development of rehabilitation directions;
- the functioning of clinical–dosimetric epidemiological registry of survivors and priority groups of medical care; and
- the improvement of the system of the establishment of the connection of diseases with the impact of ionizing irradiation and other factors of the accident.

Acknowledgements

The authors express their sincere gratitude to the academicians of the Academy of Medical Sciences of Ukraine, O.F. Vozianov, Yu. P. Zozulya, O.M. Lukyanova, A.M. Romanenko and Yu. I. Kundiev, to the corresponding members of the Academy of Medical Sciences of Ukraine, Yu. G. Antipkin and M.D. Tronko, and to Profs. V.O. Buzunov, I.A. Likhtariov, I.P. Los, M.I. Omelyanets, E.I. Stepanova, I.M. Khomaziuk, A.I. Nyagu, O.M. Kovalenko and V.A. Prilipko for making it possible to use the materials in their paper.

References

[1] National Report of Ukraine, Kiev, 2001.

[2] A.E. Romanenko, O.A. Pyatak, A.N. Kovalenko, The health of the participants of catastrophe consequences liquidation, in: A.E. Romanenko (Ed.), Chernobyl Catastrophe, 1997, pp. 441–445, Kiev.

[3] A.I. Nyagu, K.N. Loganovsky, K.L. Yuryev, L.L. Zdorenko, Psychophysiological aftermath of irradiation, Int. J. Radiat. Med. 2 (1999) 3–24.

[4] A.N. Kovalenko, Nonstochastic irradiation effects, in: A.E. Romanenko (Ed.), Chernobyl Catastrophe, 1997, pp. 458–469, Kiev.

[5] A.K. Cheban, Some aspects of thyroid system status in persons exposed to Chernobyl accident, Proceedings of an International Conference on Long-Term Consequences of the Chernobyl Disaster, Kiev, June 1–6, 1998, pp. 406–415.

[6] A.E. Romanenko, O.A. Pyatak, The health status of the evacuated people, in: A.E. Romanenko (Ed.), Chernobyl Catastrophe, 1997, pp. 439–442, Kiev.

[7] A. Romanenko, V. Bebeshko, D. Bazyka, Chernobyl disaster promotion of follow-up studies, Proceedings of Rempan-97: Coordination Meeting of WHO-Collaborating Centers in Radiation Emergency Medical Preparedness, 1997, pp. 245–250, Rio de Janeiro.

[8] N. Omelyanets, S.S. Kartashova, V.F. Torbin, Medico-demographic consequences, in: A.E. Romanenko (Ed.), Chernobyl Catastrophe, 1997, pp. 438–441, Kiev.

[9] N. Korol, Results of monitoring health effects among Chernobyl child victims, Cent. Eur. J. Public Health 43 (2) (1998) 108–111.

[10] A. Prysyazhnyuk, V.G. Gristchenko, Epidemiological study of cancer in Ukraine with reference to the Chernobyl accident, Proceedings of the 7th Symposium on Chernobyl-Related Health Effects, Tokyo, Nov. 25–26, 1998, pp. 199–228.

International Congress Series 1234 (2002) 281–291

Cancer incidence in Ukraine after the Chernobyl accident

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Abstract

We analyzed the temporal trend in cancer incidence rate in different groups of Ukrainian population affected by the Chernobyl accident using the data obtained from the following two main information sources: (1) local cancer registry, which was established in 1987 and covers 150,000 population in the most radio-contaminated areas close to Chernobyl; and (2) state registry of people affected by the Chernobyl accident. The latter registry covers 90,000 emergency workers in 1986–1987 and 50,000 evacuees from Pripyat city and 30-km zone who received different doses of radiation. The mean dose was evaluated as 100–200 mSv for emergency workers in 1986, 50–100 mSv for those in 1987, and 10–12 and 20–30 mSv for evacuees from Pripyat city and 30-km zone, respectively. The lifetime dose in residents of contaminated areas with deposition density exceeding 555 kBq/m^2 was estimated to reach 100 mSv. A significant risk of thyroid cancer due to exposure to radioactive iodine was noted, especially in children. According to the evaluation of dose distribution in Ukrainian population, about 85% of children aged below 3 years received the dose of 0.1–1.0 Gy; 60% of children aged 4–15 years and 50% of adolescents received 0.05–0.3 Gy; and 15,000 children born on 1979–1986 before the accident received more than 2 Gy. Cancer incidence in people still living in contaminated areas has shown a slow increase with time more than 10 years after the accident. Comparison of the standardized incidence ratio (SIR) in the three groups of affected people, i.e., residents of contaminated areas, emergency workers in 1986–1987, and evacuees, the periods of 1990–1993 and 1994–1997 showed a significant increase in emergency workers in 1986–1987 only. As to site-specific cancer, a significant increase in thyroid cancer incidence in the three groups of population, especially in evacuees, should be noted. Breast cancer incidence rate showed a significant

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PII: S0531-5131(01)00617-3

increase in female residents of contaminated areas and women who participated in emergency work in 1986–1987.

Keywords: Cancer incidence rate; Standardized incidence ratio; Dose of radiation; Contaminated area; Emergency worker; Evacuee; Population

1. Introduction

According to national report [1], a significant part of Ukrainian population was subjected to radiation after the Chernobyl accident. These circumstances have provoked anxiety in wide circles of population about the influence of radiation on human health, particularly on the risk of inducing malignant tumors.

Emergency workers who participated in clean-up works in 1986 and 1987 were estimated to have received highest average accumulated effective doses of 100–200 and 50–100 mSv, respectively [1]. Profound attention has to be paid for detailed surveillance of evacuees from Pripyat city and 30-km zone, whose mean doses are estimated as 10–12 and 20–30 mSv, respectively. It should be noted that the most significant accumulated collective doses were found in 11,870 individuals in a population of six large northern regions: 36,910 person-Sv, i.e., 75.3% of collective dose received by the whole population of Ukraine. Expected individual lifetime dose varied from 80 to 400 mSv in some groups of the most radio-contaminated areas.

Irradiation of thyroid gland by radioactive iodine especially at an early age gives quite a significant risk of developing thyroid cancer. Collective dose of this critical organ in children of Ukraine was estimated at 400,000 person-Gy, but in eight most radio-contaminated districts, it was 57,000 person-Gy, i.e., 14.2% of total collective dose in children. Together with the known susceptibility of the thyroid gland to induction of radiogenic tumors especially in young people, this justifies extensive epidemiological study of thyroid cancers in affected groups. Continuous surveillance for harmful health effects in these affected groups, especially the possible induction of radiogenic cancers, is important.

2. Materials and methods

The present research was undertaken to investigate a possible increase in incidence rate of malignant neoplasms after irradiation of large parts of Ukrainian population due to the Chernobyl accident. It was conducted in three main groups of affected population: residents of the most radio-contaminated areas, emergency workers in 1986–1987, and evacuees from Pripyat city and 30-km zone.

As to residents of the most radio-contaminated areas, we noted that the local cancer registry was set up in 1987 and that retrospective and prospective studies have been conducted to identify all cancer cases diagnosed since 1980 in the four districts: Naroditchy and Ovrutch districts of Zhitomir region, and Ivankov and Polesskoye districts of Kiev region. Furthermore, all cancer cases in the former Chernobyl district in 1981–1985 were also reconstructed and included in the study group. The population of these five districts at the time of the accident was 274,000 including 59,200 children aged 0–14 years. In 1997, the population of the four districts, excluding practically unpopulated Chernobyl district, was 132,000 including 23,400 children. All medical documents including urgent notification of new cancer cases and death certificates were collected from all medical institutions which diagnosed and treated the patients. All records were cross-checked to avoid duplication before compiling the final file. A total of 9987 new cancer cases have been registered since 1980.

Annual age-specific and age-adjusted (by direct method) incidence rates were calculated for 1980–1997 and were compared with corresponding data for the whole Ukraine and for the Kiev and Zhitomir regions which include the districts of interest. The standard age structure was constructed on the basis of the 1979 all-union census population.

State registry data were used for the study of cancer incidence in emergency workers in 1986–1987, and evacuees from Pripyat city and 30-km zone. We analyzed the data of 83,965 emergency workers in 1986–1987 living in Dnepropetrovsk, Donetsk, Kiev, Lugansk, and Kharkov regions as well as Kiev city, and 50,437 evacuees resettled in the whole territories of Ukraine. The indirect method of standardization was used for the analysis. Because of the relatively small number of subjects and age-specific cancer incidence rate of Ukrainian population in 1990–1996, it was used as the standard rate in the calculation of the standardized incidence ratio (SIR).

3. Results

Cancer incidence rates in various territories are illustrated in Fig. 1. Throughout 1980–1997, the cancer incidence rate was lower in people still living in the most contaminated areas than in the entire Ukraine, Kiev region, and Zhitomir region. The temporal trend in cancer incidence rate, however, was similar for the four territories: the respective annual cancer incidence rates were around a gradually increasing line throughout the entire period. Such a temporal change is characteristic of the entire Ukraine as well as radio-contaminated regions and most of the contaminated small districts. No significant difference was noted among regression coefficients, which estimates the annual increase.

Comparison of the standardized incidence ratios (SIR) in different groups of affected population in periods 1990–1993 and 1994–1997 (Table 1) indicated no significant increase in cancer incidence rates either in evacuees or residents of the most contaminated areas, while it indicated a significant increase with the emergency workers in 1986–1987. A feature of the temporal trend in the cancer incidence in evacuees is that a significant increase with time was observed in young age groups while no such increase was observed in other age groups.

The greatest interest at present, which is more than 10 years after the Chernobyl accident, is malignant tumors such as breast, lung, stomach, bowels, ovary cancers, etc., as well as lymphoma and leukemia which could be attributed to prolonged effect of ionising radiation.

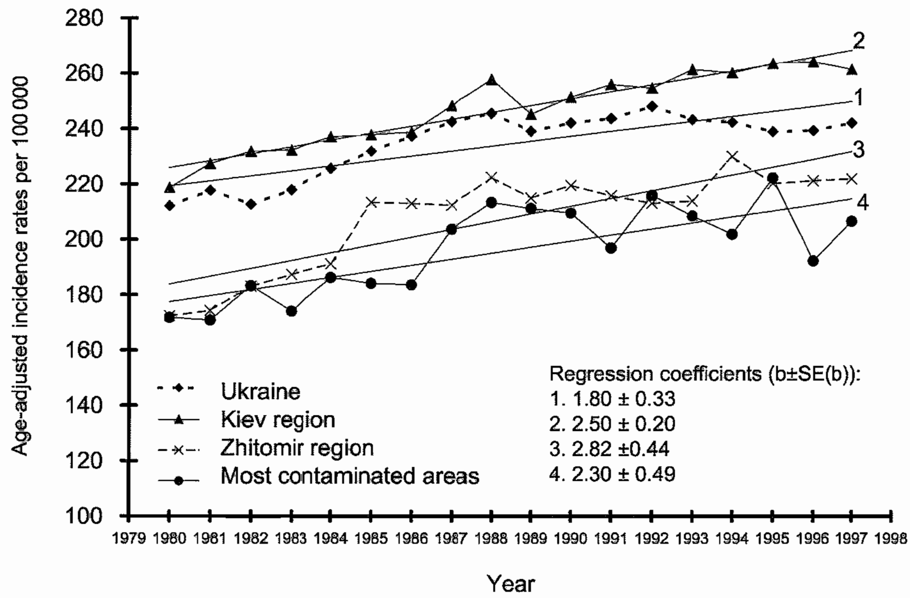

Fig. 1. Dynamics of cancer incidence rates in the Ukraine, Kiev region, Zhitomir region, and the areas most contaminated with radionuclides. Males and females.

Temporal fluctuation is notable in the leukemia and lymphoma incidence rate especially in the most radio-contaminated areas (Fig. 2). It should also be noted that the leukemia and lymphoma incidence rate increased in 1987–1991 and then decreased. Since the minimum

Table 1
Standardized incidence ratio (SIR) of all cancers (ICD-10, 140–208) in different groups of Ukrainian population affected by the Chernobyl accident

Observation group and period	Person-years of observation	Observed number of cases	Expected number of cases	SIR	95% CI
Residents of contaminated territories					
1990–1997	1,211,132	3963	4890	81.1	78.6–83.6
1990–1993	654,501	2143	2607	82.2	78.8–85.7
1994–1997	556,631	1820	2283	79.7	76.1–83.4
Emergency workers 1986–1987 (males)					
1990–1997	577,536	1496	1354	110.5	104.9–116.1
1990–1993	263,084	538	443	121.5	111.2–131.8
1994–1997	314,452	958	911	105.1	98.5–111.8
Evacuees from 30-km zone					
1990–1997	408,882	870	1234	70.5	65.8–75.2
1990–1993	208,805	432	618	69.9	63.3–77.8
1994–1997	200,077	438	616	71.1	64.5–77.8

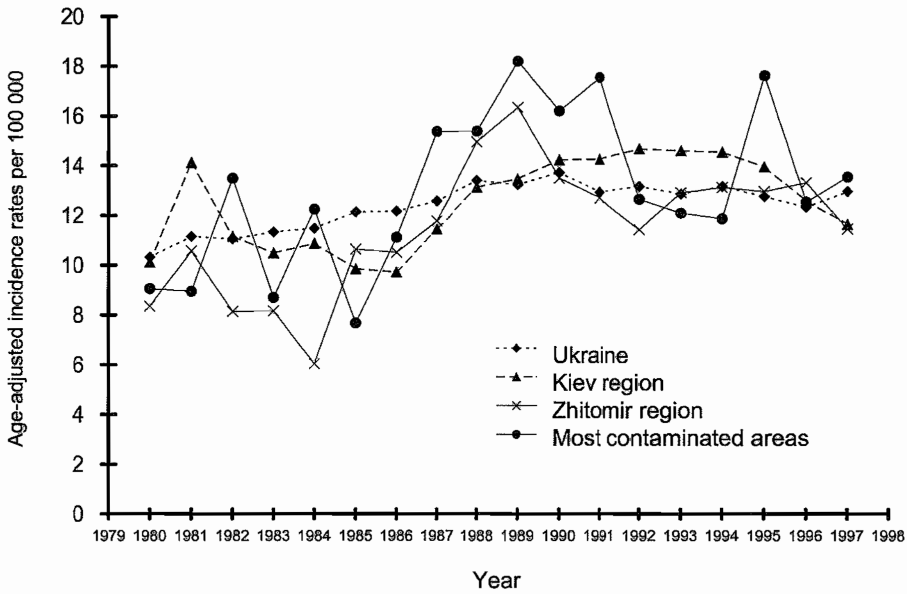

Fig. 2. Dynamics of leukemia and lymphoma incidence rates in the Ukraine, Kiev region, Zhitomir region, and the areas most contaminated with radionuclides. Males and females.

latent period for these diseases is 2 years [2] and since the incidence is expected to reach the peak in 6–8 years, the observed transient increase would be caused not by radiation but screening. The regression coefficient estimates (±standard errors) were 0.14±0.03, 0.19±0.07, 0.31±0.10, and 0.31±0.13 for the entire Ukraine, Kiev region, Zhitomir region, and most contaminated area, respectively; no significant difference was noted in the regression coefficient among the territories.

Comparison of the leukemia and lymphoma incidence rate in the extended period showed, however, significantly much higher levels in the periods 1986–1991 ($P<0.01$) and 1992–1997 ($P<0.05$) as compared with the pre-accidental periods (1980–1985) (Table 2). In the similar analysis of respective sub-types of these diseases, a significant increase was observed in the lymphatic leukemia incidence in 1986–1991 ($P<0.05$) but the disease is not radiogenic [3]. Similarly, a significant increase was observed in the myeloid leukemia incidence rate in 1986–1991 ($P<0.01$). However, a relatively large standard error in 1980–1985 forestalls drawing conclusion. A gradual increase was observed in the lympho- and reticulosarcoma incidence rate, which was significantly higher in 1992–1997 ($P<0.05$) as compared with the period 1980–1985. However, due to the large-scale migration of people from contaminated areas, there is concern that some members of the group of highest potential risk may have been lost for follow-up.

The radiation origin of the dramatic increase in thyroid cancer incidence rates (Fig. 3) raises no doubt these days. In Ukraine, on the whole, this increase was approximately 2.0 times the above spontaneous expected level in male and female populations. Fig. 4 indicates that the increase in Kiev city and Kiev region, to which 70% of the population of

Table 2
Age-adjusted annual incidence rates of leukemia and lymphoma in the most contaminated areas during the three periods of (I) 1980–1985, (II) 1986–1991 and (III) 1992–1997

ICD-9 code	Diseases	(I) 1980–1985	(II) 1986–1991	$t_{I,II}$ [a]	(III) 1992–1997	$t_{I,III}$ [b]
200–208	Leukemia and lymphoma	10.12±0.75	15.63±1.06	4.25, $P<0.01$	13.41±1.10	2.48, $P<0.05$
200, 202	Lympho-and reticulosarcoma	1.84±0.33	2.70±0.41	1.64, $P>0.05$	3.70±0.58	2.77, $P<0.05$
201	Hodgkin's desease (Lymphogranulematosis)	1.82±0.34	2.47±0.48	1.12, $P>0.05$	2.10±0.48	0.48, $P>0.05$
203	Multiple myeloma and immunoproliferative neoplasms	0.54±0.16	1.03±0.25	1.66, $P>0.05$	0.78±0.22	0.88, $P>0.05$
204	Lymphatic leukemia	3.08±0.40	4.93±0.59	2.59, $P<0.05$	2.97±0.49	0.17, $P>0.05$
205	Myeloid leukemia	0.49±0.17	1.99±0.41	3.40, $P<0.01$	1.06±0.30	1.68, $P>0.05$
206–208	Other leukemia	2.35±0.36	2.51±0.41	0.29, $P>0.05$	2.81±0.53	0.71, $P>0.05$

[a] t-value and P-value as compared the incidence in the period II to that in period I.
[b] t-value and P-value as compared the incidence in the period III to that in period I.

Pripyat city and 30-km zone evacuated, was 5 and 6 times, respectively. The regression coefficient estimates (±standard errors) were 0.17±0.01, 0.61±0.10, 0.19±0.05, 0.50±0.06, and 0.43±0.10 for the entire Ukraine, Kiev region, Zhitomir region, Kiev

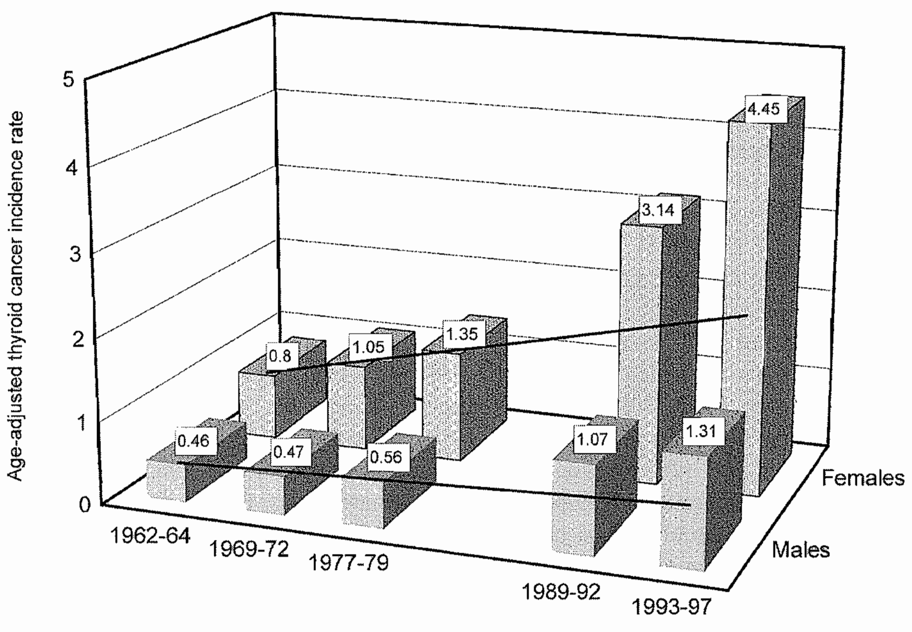

Fig. 3. Age-adjusted annual thyroid cancer incidence rates in the Ukraine by sex and observation period.

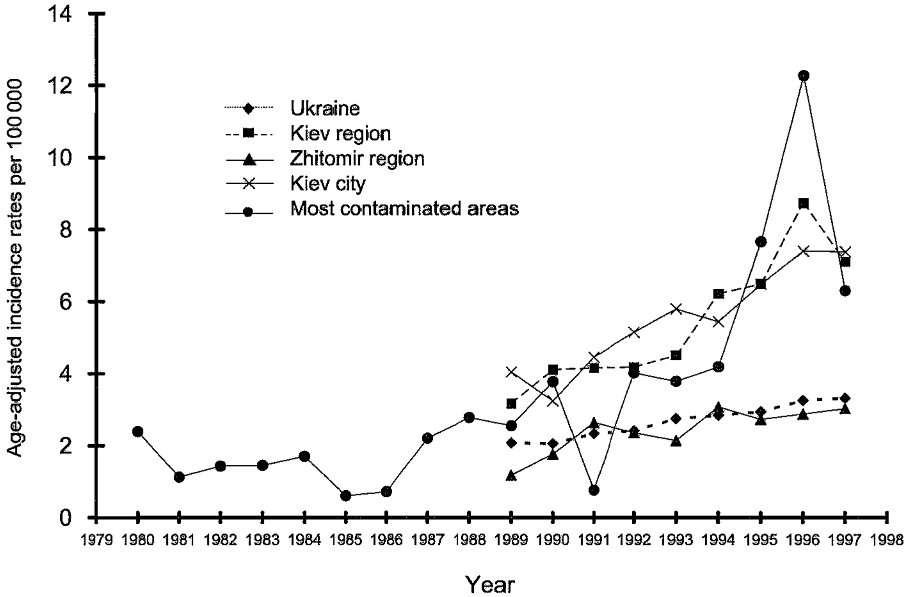

Fig. 4. Dynamics of thyroid cancer incidence rates in the Ukraine, Kiev region, Zhitomir region, and the areas most contaminated with radionuclides. Males and females.

city, and most contaminated area, respectively. The dramatic increase in thyroid cancer incidence rate occurred in 1996 in the most contaminated areas.

Comparative analysis of thyroid cancer incidence in different groups of affected population (Table 3) showed the most significant exceeding of national level in evacuees

Table 3
Standardized incidence ratio (SIR) of thyroid cancer (ICD-9, 193) in different groups of Ukrainian population affected by the Chernobyl accident

Observation group and period	Person-years of observation	Observed number of cases	Expected number of cases	SIR	95% CI
Residents of contaminated territories					
1990–1997	1,211,132	72	41.7	172.9	135.2–215.1
1990–1993	654,501	24	22.4	107.2	68.6–154.4
1994–1997	556,631	48	19.3	249.1	183.6–324.6
Emergency workers 1986–1987 (males)					
1990–1997	577,536	37	8.4	442.7	300.0–585.3
1990–1993	263,084	13	3.3	393.0	179.4–606.6
1994–1997	314,452	24	5.1	475.2	285.1–665.4
Evacuees from 30-km zone					
1990–1997	408,882	66	12.9	513.4	389.6–637.3
1990–1993	208,805	23	6.4	362.0	214.1–510.0
1994–1997	200,077	43	6.5	661.4	463.7–859.1

(in 3.6 and 6.6 times in 1990–1993 and 1994–1997, respectively), emergency workers (in 3.9 and 4.8 times in 1990–1993 and 1994–1997, respectively). In the population of contaminated areas, statistically significant 2.5-fold increase was registered in 1994–1997.

As to other forms of malignancy incidence rates, attention should be drawn to female breast cancer, which belongs to radiosensitive form of cancer. In the most contaminated areas, female breast cancer incidence rates were relatively stable during 1980–1992 (Fig. 5) though lower than in Ukraine as a whole or in regions that include contaminated areas. The regression coefficient estimates (±standard errors) were 0.76±0.04, 0.73±0.10, and 0.89±0.09 for the entire Ukraine, Kiev region, and Zhitomir region, respectively. For the most contaminated areas, however, the regression coefficient estimates (±standard errors) differed by period: 0.01±0.25 in 1980–1992; 1.11±1.08 in 1993–1997; and 0.72±0.20 in 1980–1997.

In 1993–1997, however, an increase in rate (Table 4) occurred in the most contaminated areas, the rate now corresponds more closely to the rate typical of Ukraine as a whole. A statistically significant increase in breast cancer incidence was also observed in female emergency workers in 1986–1987 during 1994–1997, but not during 1990–1993 (Table 4). In evacuees, a small increase (1.3-fold) is suggested.

Special attention has to be paid to children as the most vulnerable to radiation group of population and to incidence rate of individual forms of cancer in this group such as thyroid cancer, leukemia, and lymphoma. During 1980–1997, in the most radio-contaminated areas, some fluctuations were observed in cancer incidence rate in children population because of the smallness in number of observed cases. In this situation, the importance of each of them increases. The completeness or lack of quality of registration could influence a value of incidence rate in large degrees (Table 5).

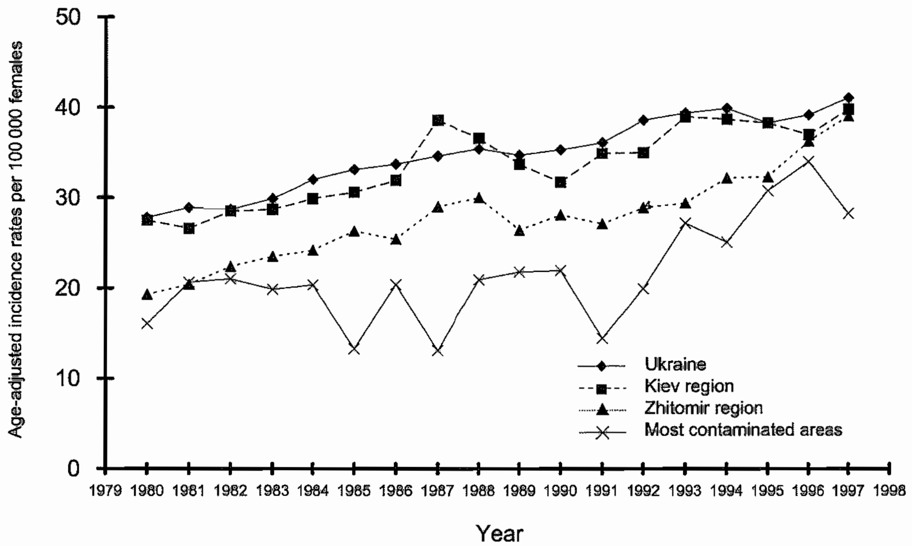

Fig. 5. Dynamics of breast cancer incidence rates in the Ukraine, Kiev region, Zhitomir region, and the areas most contaminated with radionuclides.

Table 4
Standardized incidence ratio (SIR) of breast cancer (ICD-9, 174) in different groups of Ukrainian population affected by the Chernobyl accident

Observation group and period[a]	Person-years of observation	Observed number of cases	Expected number of cases	SIR	95% CI
Residents of contaminated territories[b]					
1993–1997	389,645	162	107.8	150.3	127.1–173.4
Clean-up workers 1986–1987[c]					
1990–1997	39,188	44	29.1	151.2	106.5–195.8
1990–1993	15,913	12	10.9	110.2	47.9–172.6
1994–1997	23,275	32	18.2	175.6	114.8–236.5
Evacuees from 30 km zone[b]					
1990–1997	235,072	72	52.3	137.7	105.9–169.5
1990–1993	119,915	37	25.7	143.9	97.5–190.2
1994–1997	115,157	35	26.6	131.7	88.1–175.3

[a] Because of the variation by territory in the breast cancer incidence in the Ukraine, SIR was calculated on the basis of two standards:local and national.
[b] Local standard, 1980–1992.
[c] National standard, 1990–1996.

It should be pointed out that in 1980–1985, the level of morbidity did not significantly differ from expected national level. Significant increase was observed in 1986–1991 and 1992–1997. In the last 2 years, the difference of morbidity was insignificant.

As to individual forms of childhood cancer, the most significant attention has to be paid to thyroid cancer. In 1980–1985, no case of this disease was observed in the territory of interest. First cases of thyroid cancer were observed in 1990. However, significant preponderance of observed number in comparison with expected one was registered in 1992–1997—in 18.2 times.

Temporal variation in the lymphoma and leukemia incidence rate was quite large. However, in 1980–1985, it did not exceed expected level. In 1986–1991, a significant excess of observed cases over expected ones was registered as 2.5 times. However, in the subsequent period of 1992–1997, the level of morbidity did not significantly differ from national data. This situation is similar for leukemia only (ICD-9, 204–208). Attention should be paid on the fact that the peak of incidence was notified in 1990, i.e., 4 years after the Chernobyl accident, followed by a sharp decrease in the incidence in the subsequent years. Observed number of cases exceeded the expected one in 3.2 times (statistically significant difference). In 1992–1997, SIR was not significant.

As to other forms of malignancy incidence rate, it did not significantly differ from the national level.

Thus, only thyroid cancer has significantly increased in 1992–1997. One explanation of this situation could be that the peak of the leukemia and lymphoma incidence has passed. Another hypothesis is the impact of out-migration of the most risky group of population. Effective functioning of the state registry of persons affected by the Chernobyl accident is therefore very important. Application of cohort approach to this group of population is very important because of ageing. However, SIRs for the child population at

Table 5
Standardized incidence ratio (SIR) of cancer in children (0–14) in areas most contaminated with radionuclides

Site of tumors (ICD-9 code) and observation period	Person-years of observation	Observed number of cases	Expected number of cases	SIR	95% CI
All cancers (140–208)					
1980–1985	337,076	44	36.48	120.62	84.98–156.26
1986–1991	209,337	44	22.69	193.95	136.64–251.26
1992–1997	150,170	31	16.26	190.62	123.51–257.72
1992–1997 (5–24 years of age)	196,027	43	29.52	145.68	102.14–189.23
Leukemia and lymphoma (200–208)					
1980–1985	337,076	21	17.28	121.51	69.54–173.49
1986–1991	209,337	27	10.75	251.11	156.39–345.84
1992–1997	150,170	11	7.72	142.49	58.28–226.69
1992–1997 (5–24 years of age)	196,027	12	12.43	96.54	41.92–151.16
Leukemia (204–208)					
1980–1985	337,076	19	10.88	174.68	96.13–253.22
1986–1991	209,337	22	6.78	324.35	188.82–459.89
1992–1997	150,170	7	4.87	143.70	37.25–250.15
1992–1997 (5–24 years of age)	196,027	5	5.29	94.59	11.68–177.51
Thyroid cancer (193)					
1980–1985	337,076	0	1.13	0.00	0.00–0.00
1986–1991	209,337	2	0.69	289.84	(−111.86)–691.53
1992–1997	150,170	9	0.49	1824.77	632.59–3016.95
1992–1997 (5–24 years of age)	196,027	14	1.33	1054.52	502.13–1606.92
All cancers except leukemia, lymphoma, and thyroid cancer (140–208 excluding 200–208, 193)					
1980–1985	337,076	23	18.07	127.29	75.27–179.31
1986–1991	209,337	15	11.24	133.40	65.89–200.91
1992–1997	150,170	11	8.05	136.65	55.89–217.40
1992–1997 (5–24 years of age)	196,027	17	15.76	107.88	56.60–159.17

the time of the accident (aged 5–24 years in 1992–1997) do not significantly differ from the expected number of cases.

4. Discussion and conclusions

Similar trends in the cancer incidence rates were apparent in different Ukrainian population groups directly affected by the Chernobyl accident (those that still reside in the most contaminated districts, emergency workers and evacuees). There is an excess of thyroid cancer [3]. For leukemia and lymphomas, female breast cancer, and solid cancers, there are suggestions of increases. Further monitoring is required to verify this along with evaluation of the effects of screening and improved registration quality. The small number of cases of certain types of cancer and the confounding effects of out-migration means that cancer monitoring and surveillance should include not only contaminated districts but outside regions where such residents relocated. The apparent increases, at least in part, may reflect differences in case ascertainment between these groups and the general population of Ukraine as opposed to a radiation-related effect [3].

Resolution of these questions will be aided by utilizing state registry of persons affected by the Chernobyl accident and by data linkage between this registry and the regional cancer registries responsible for collection of information about cancer cases in their particular territories. If this information is to be used for risk assessment, it is important to obtain information about doses to individuals for the purposes of late risk assessments.

References

[1] V. Durdinets (Ed.), Fifteen Years After the Chernobyl Catastrophe. Experience of Overcoming: National Report of Ukraine, Chernobylinform, Kiev, 2001 (in Ukrainian).

[2] W.K. Sinclair, The international role of RERF, RERF Update 8 (1) (1996) 6–8.

[3] United Nations Scientific Committee on the Effects of Atomic Radiation, Sources and Effects of Ionizing Radiation. Volume I: Sources; Volume II: Effects. 2000 Report to the General Assembly with Scientific Annexes, United Nations, New York, 2000.

International Congress Series 1234 (2002) 293–300

Thyroid cancer among children and adolescents of Belarus exposed due to the Chernobyl accident: dose and risk assessment

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Keywords: Thyroid cancer; Chernobyl accident; Assessment

1. Introduction

The accident at the Chernobyl Nuclear Power Plant resulted in the release to the atmosphere of tremendous amount of ^{131}I (about 1760 PBq), short-lived and long-lived iodine radionuclides as well [1,2]. The released amount of iodine radionuclides significantly exceeded the releases from all known accidents at nuclear power plants. Meteorological conditions of airflow spread during the first weeks following the accident determined the formation of radioactive fallout in northwest and northeast directions from the Chernobyl Nuclear Power Plant, and as a result, vast territories of Belarus were contaminated by iodine radionuclides. The density of contamination by ^{131}I in five out of six regions of Belarus was from 0.2 to 37 MBq/m^2 [3].

The affliction of the thyroid by radioactive iodine in the early period of the accident caused a serious danger to the health state of the Belarussian population. Particularly, it resulted in the increased development of malignant thyroid malformations. It is known that iodine is the most important component of thyroid hormones. It is quickly accumulated by the thyroid and relatively slowly deduced from it. This is the reason why even if small amounts of iodine radionuclides entered the body, a high level of absorbed dose is formed in the thyroid [4].

Risk assessment of radiation-induced cancers requires a period of time following the accidental exposure during which the latent period will be finished and a certain amount of

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PII: S0531-5131(01)00618-5

excess cancer cases may be revealed. During the last 15 years, studies of stochastic consequences of the Chernobyl accident among the population of Belarus have allowed the estimation of the risk coefficient only for radiation-induced thyroid cancer. There is still not enough data for the conclusion about the observed excess of cancer cases since the end of the latent period (10 years is assumed as a latency for solid tumors). Risk estimation of radiation-induced diseases caused by the Chernobyl accident based on obtained data from registered cases would allow us to make more precise prognosis for late health radiation effects.

The current paper presents the results of risk assessment of thyroid cancer development for the whole cohort of 0–18 years of age at the time of the accident, considering specificity of sex and age at the time of exposure using the data of dose levels and incidence rate throughout the whole territory of the republic.

2. Materials and methods

2.1. The gender–age structure of the population of Belarus in 1986

The necessary demographic information has been obtained as a result of the retrospective estimation of the gender–age structure of the population for 1986. The calculations were made on the basis of the data concerning the total number of inhabitants with regard to the settlements of the country in 1989, the year of the general census of the population and the nearest one to 1986 [5,6].

2.2. Collection and analysis of information about thyroid cancer cases of the inhabitants of Belarus exposed to radiation at the age of 0–18

The medical history data of the patients, who underwent treatment in the Republican Scientific–Practical Center of Thyroid Oncopathology, as well as the Belarussian Cancer Register data were the information source of the first revealed thyroid cancer cases. The examined cohort included the people exposed to radiation at the age of 0–18 (born from 1 January 1968 to 26 April 1986).

2.3. Reconstruction of thyroid doses from ^{131}I

The reconstruction of the thyroid doses was made based on the radioecological model [7,8] using refined values of the parameters [9,10]. The main principle of clarifying the values was to use region-specific values for the particular parameter rather than the values averaged all over Belarus.

3. Results and discussion

The analysis of available quantitative and qualitative data of direct measurements of exposure dose rate above the thyroid performed in May–June 1986 for a limited part of the population (Table 1) showed the necessity of using alternative methods of dose calculation from incorporated ^{131}I.

It is important to emphasize that in all persons with thyroid cancers revealed until the end of 2000, less than 8% have information about thyroid dose reconstruction based on direct measurements. For the rest of the patients and for the Belarussian population, another method of thyroid dose reconstruction should be applied.

The ECOSYS-87 radioecological model [7] was suggested as an alternative method for thyroid dose reconstruction for the affected population of Belarus. Parameters used in the radioecological model were adapted to Belarussian conditions. The main principle of parameter clarification was to refuse the usage of averaged estimates throughout Belarus and the calculation of the specific parameters for the particular regions. The following important parameters of the model were determined according to the respective local conditions: ratio between ^{131}I and ^{137}Cs deposition, initial interception factor, yield of pasture grass and age-dependent milk consumption for the rural and urban population.

While adapting the radioecological model to the conditions existing in Belarus at the time of the accident, it was accepted that the consumption of locally produced milk was the only way of radioiodine intake. It could be explained by the fact that during the first days following the accident the inhalation intake of radioiodine was one of the most important ways for thyroid exposure dose formation only for the population who continued living on contaminated territories close to the Chernobyl Nuclear Power Plant, and for the majority of the population, consuming foodstuffs (milk and leafy vegetables) locally produced was the most important way of radioiodine intake in the body. In the territories where dry fallout took place and where people are permanently residing in the contaminated territory, in the lack of countermeasures, the contribution to the dose from inhalation to the total dose of thyroid exposure was from 2% to 10%.

Taking into account the seasonal factors, it was accepted that the radioiodine intake with green leafy vegetables was much less than that with milk. In this case, according to

Table 1
Number of Belarussians aged 0–18 years in 1986 who underwent direct measurement of the dose rate of the thyroid gland in May–June 1986

Region	Number of people aged 0–18 years in 1986	Population with thyroid dose calculated on the basis of direct measurements	
		Number of people	Proportion (%) in the total population aged 0–18 years in 1986
Brest	404017	0	0
Vitebsk	354655	0	0
Gomel	468092	27463	5.9
Grodno	306784	0	0
Minsk[a]	422121	0	0
Minsk City	424455	7177	1.7
Mogilev	342685	4548	1.3
Belarus	2722809	39188	1.4

[a] Excluding Minsk City.

the radioecological model, the dose to the thyroid could be calculated in the following way (fallouts are considered as single and dry):

$$D = \mathrm{DF}V_{\mathrm{m}}\mathrm{GD}_{131}f_{\mathrm{w}}/YI_{\mathrm{g}}\mathrm{TF}_{\mathrm{m}}\lambda_{\mathrm{b}}/(\lambda_{\mathrm{b}}-\lambda_{\mathrm{w+d}})\int\{\exp(-(\lambda_{\mathrm{w+b}}+\lambda_{\mathrm{r}})t) - \exp(-(\lambda_{\mathrm{b}}+\lambda_{\mathrm{r}})t)\}\mathrm{d}t,$$

where: DF — age-dependent dose factor, Sv/Bq; V_{m} — amount of daily consumed milk, l/day; GD_{131} — density of ^{131}I fallout, kBq/m^2; f_{w} — initial interception factor of ^{131}I by the grass, relative units; Y — grass productivity, kg/m^2; I_{g} — consumption of grass by the cow, kg/day; TF_{m} — ^{131}I transfer factor from the grass to the milk, l/day; λ_{b} — biological elimination rate constant for the milk from ^{131}I, day; $\lambda_{\mathrm{w+d}}$ — weathering and growth dilution rate constant for the grass, day; λ_{r} — constant of radioactive decay, day; and t — time period from the beginning of the fallout, day.

Using a radioecological model with adopted parameters for Belarussian conditions, the reconstruction of the absorbed thyroid doses from ^{131}I for the population of all Belarussian settlements exposed at the age of 0–18 years was conducted. The average levels of the dose for each age within the mentioned age group were performed. According to this estimation, about 98% of the cohort have doses less than 1 Gy, and only 2% have doses exceeding 1 Gy (Fig. 1).

The specific feature of the radiation accident at the Chernobyl Nuclear Power Plant is its patchiness and irregularity of contamination of the territory by radionuclides which resulted in a great variation of the average thyroid doses received by the population of the different regions. The population of the Gomel region received the highest levels of thyroid doses. The most affected districts were Khoiniki, Bragin, Narovlya and Vetka, where the average doses in the population group of 0–18 years old exceeded 1 Gy. For the

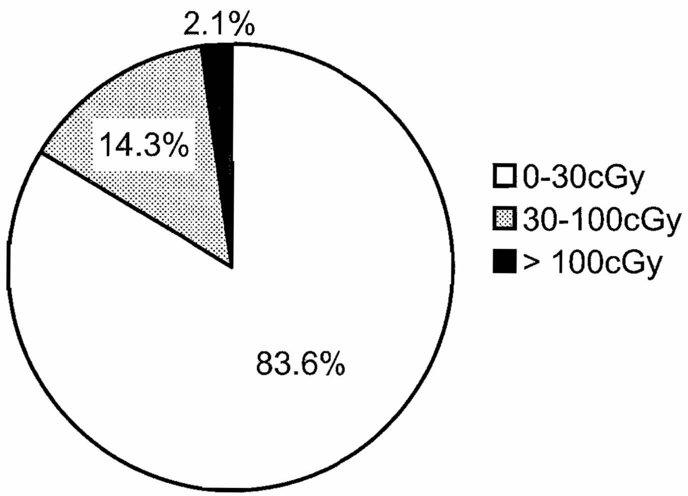

Fig. 1. Percent distribution of the population aged 0–18 years at the time of the accident by the level of thyroid dose from ^{131}I.

population in the rest of the regions of the country, the levels of thyroid doses were within 1 Gy. For the population within the same region, the levels of dose vary depending on the age of the exposed group. The distinction between the doses within one settlement conditioned only by the age at the time of the accident reached the correlation of 1:5.5.

Taking into account the levels of thyroid doses for the patients with thyroid cancer, the distribution of the cases through the dose intervals is presented in the following way: 37.7% cases of thyroid cancer occurred in the group of population who received a dose of up to 30 cGy, 45.4%, 30–100 cGy and 16.9%, more than 1 Gy (Fig. 2).

While comparing Figs. 1 and 2, which present the distribution of the Belarussian population in the age cohort of 0–18 years at the time of exposure by dose intervals and distribution of the thyroid cancer cases among this cohort, it is evident that the highest thyroid cancer incidence is observed among the population that belongs to the high dose group. Thus, only 2.1% of the population fell in the dose interval exceeding 1 Gy. Meanwhile, the percentage of patients in this dose group is about 17%. At the same time, the percentage of the population in the dose group 0–30 cGy is 83.6% and the percentage of patients from this dose group is 45.4%. A comparison of these distributions is presented in Fig. 3.

Depending on the location at the time of the accident, the thyroid cancer incidence could be presented in the following way: the maximal cumulative incidence rate for the post-accidental period for the cohort of 0–18 years old is observed among the children who lived at the time of the accident in the Gomel region at 101.6, and in the Brest region, at 53.2. The Grodno region, Minsk region and Mogilev region have approximately equal rates of 22.2, 22.4, and 20.2, respectively, and in the Vitebsk region, 12.8 per 10^5 of the population. Table 2 presents the distribution of the thyroid cancer cases by calendar years in different regions of the republic for patients whose place of residence at the time of the accident is known.

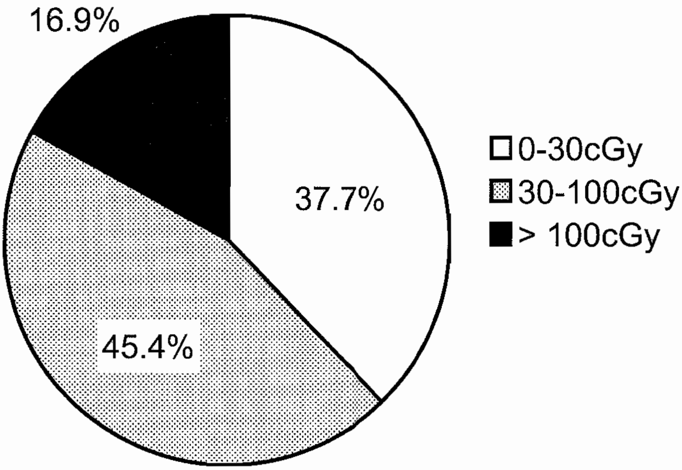

Fig. 2. Percent distribution of the people with thyroid cancer aged 0–18 years at the time of the accident by the level of thyroid dose from ^{131}I.

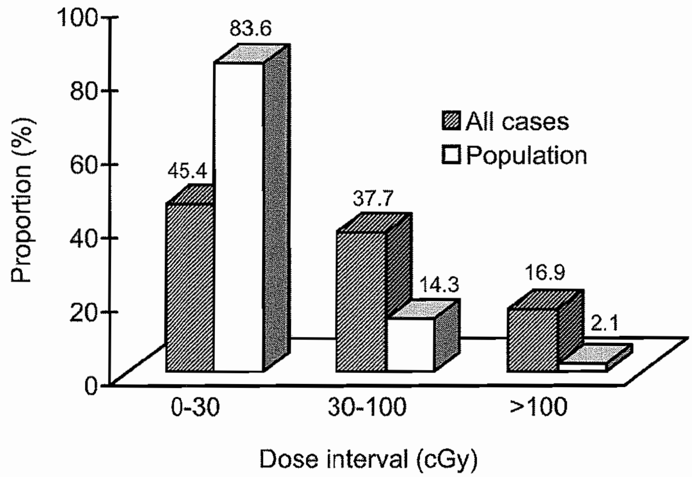

Fig. 3. Percent distribution of the Belarussian population and people with thyroid cancer by thyroid dose intervals.

In the republic following the accident at the Chernobyl Nuclear Power Plant, thyroid cancer incidence rates exceed the expected age-specific incidence rates for both boys and girls. The highest rates of cumulative incidence for the post-latent period (since 1990) are observed among the population who received the highest doses to the thyroid from ^{131}I (Figs. 4 and 5).

We calculated the number of person-years at risk and the excess thyroid cancer incidence for the population with thyroid doses in the intervals < 0.3, 0.3–0.6, 0.6–1.0,

Table 2
Number of thyroid cancer cases after the Chernobyl accident by year and region of residence at the time of the accident

Year	Region						Total
	Brest	Vitebsk	Gomel	Grodno	Minsk	Mogilev	
1986	0	1	0	1	1	0	3
1987	0	1	6	2	2	1	12
1988	1	0	3	1	4	0	9
1989	0	1	7	2	3	1	14
1990	9	2	18	0	7	2	38
1991	3	2	54	6	7	5	77
1992	21	10	45	11	9	4	100
1993	31	3	52	3	19	6	114
1994	32	5	60	10	25	14	146
1995	32	5	68	6	18	8	137
1996	42	5	67	8	25	9	156
1997	20	7	75	9	28	11	150
1998	40	5	60	8	36	16	165
1999	35	9	91	5	30	33	203
2000	34	5	81	6	22	23	171
Total	300	61	687	78	236	133	1495

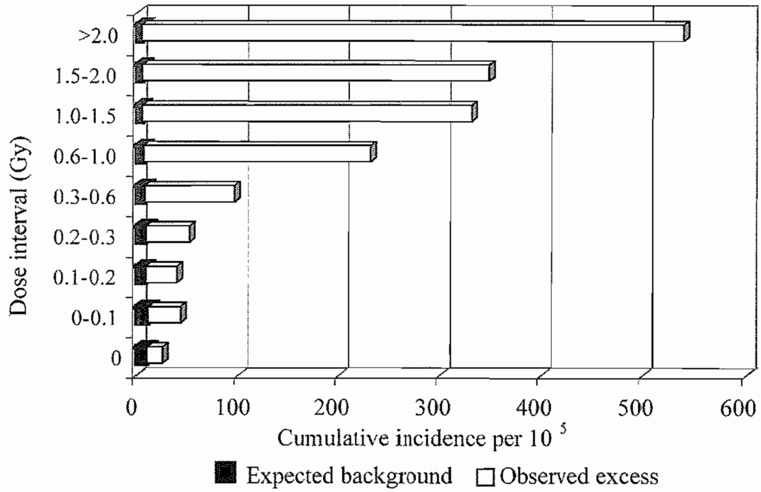

Fig. 4. Cumulative incidence rate for the girls exposed at the age of 0–18 years.

1.0–2.0 and >2.0 Gy. With the use of the obtained parameters, we performed the calculation of the excess absolute and excess relative risk coefficients per unit of dose (Table 3) [6].

The absolute risk coefficient calculated for the boys and girls who were exposed to the radiation at the age of 0–18 years is 1.93 (1.79/2.06) per 10^4 person-year-Gy, and the relative risk coefficient is 37.66 (35.06/40.26) per Gy. The boys–girls ratio with regard to the absolute risk coefficient is 1:2, yet it fluctuates within this age cohort according to the thyroid dose.

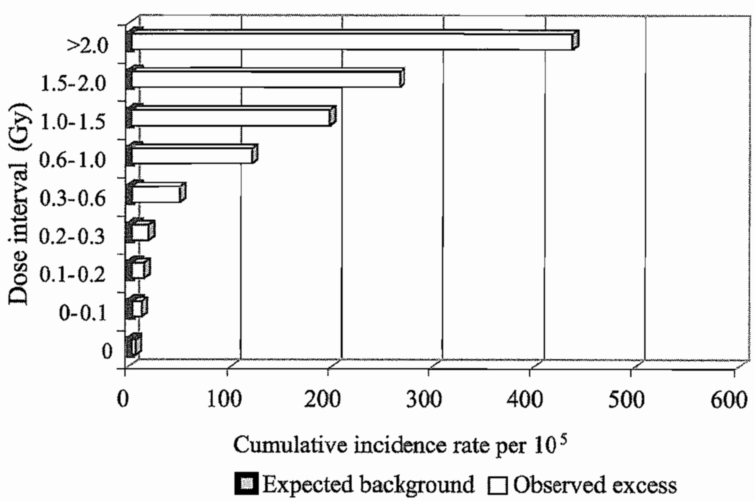

Fig. 5. Cumulative incidence rate for the boys exposed at the age of 0–18 years.

Table 3
Results of the risk assessment for radiation-induced thyroid cancer for the population of Belarus exposed at the age of 0–18 years

Parameters	Boys	Girls	Both genders
EAR (10^4 person-years-Gy) (95% CI)	1.33 (1.17–1.49)	2.63 (2.40–2.86)	1.93 (1.79–2.06)
ERR (Gy) (95% CI)	55.03 (48.6–61.5)	32.39 (29.6–35.16)	37.66 (35.06–40.26)

Since the thyroid cancer incidence rate within the cohort under investigation does not have a tendency to decrease yet, it is a necessary to continue the study and perform the re-evaluation of the data on a regular basis.

References

[1] L. Devell, S. Guntay, D.A. Powers, The Chernobyl reactor accident source term: development of a consensus view, NEA/CSNI/R, (95) (1996) 24.
[2] M. Dreicer, R. Aarkrog, R. Alexakhin, et al., Consequences of the Chernobyl accident for the natural and human environments: one decade after Chernobyl, Summing Up the Consequences of the Accident, Proc. of an Internat. Conf., Vienna, 1996, IAEA, Vienna, 1996, pp. 319–366, TI/PUB/1001.
[3] E. Konoplya, I. Rolevich (Eds.), The Chernobyl Catastrophe Consequences in the Republic of Belarus, National Report, Ministry of Emergencies and Population Protection from the Chernobyl NPP Catastrophe Consequences, Academy of Sciences of Belarus, Minsk, 1996, pp. 7–9 (In Russian).
[4] E.P. Demidchik, A.F. Tsyb, E.F. Lushnikov, Thyroid Cancer Among Children, Medicine, Moscow, 1996, 206 pp. (in Russian).
[5] Population of Belarus, Statistical Report, Ministry of Statistics and Analysis Republic of Belarus, Minsk, 1995, 447 pp. (In Russian).
[6] J. Kenigsberg, E. Buglova, A. Golovneva, J. Kruk, Thyroid cancer risk in Belarus after Chernobyl accident: reconstruction of individual thyroid dose and thyroid cancer, Proc. of Ninth Symposium on Chernobyl-Related Health Effects, Long-Term Health Effects of Chernobyl Accident on Children and Liquidators: Summing Up Epidemiological Studies, Radiation Effects Association, Tokyo, Japan, 2000, pp. 71–86.
[7] H. Muller, G. Prohl, ECOSYS-87: a dynamic model for assessing radiological consequences of nuclear accidents, Health Phys. 64 (1993) 232–252.
[8] V. Drozdovitch, G. Goulko, V. Minenko, et al., Thyroid dose reconstruction for the population of Belarus after the Chernobyl accident, Radiat. Environ. Biophys. 36 (1997) 17–23.
[9] P. Jacob, Y. Kenigsberg, I. Zvonova, et al., Childhood exposure due to the Chernobyl accident and thyroid cancer risk in contaminated areas of Belarus and Russia, Br. J. Cancer 80 (9) (1999) 1461–1469.
[10] P. Jacob, Y. Kenigsberg, G. Goulko, et al., Thyroid cancer risk in Belarus after the Chernobyl accident: comparison with external exposures, Radiat. Environ. Biophys. 39 (2000) 25–31.

International Congress Series 1234 (2002) 301–306

Reconstruction of thyroid dose after the Chernobyl accident

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Abstract

The main stages of the work conducted and the results of thyroid dose reconstruction for the Belarusian residents are presented in the paper. The problems relating to the systematic errors which occurred during in vivo monitoring of ^{131}I-thyroid content are considered. The importance of using the most adequate model of thyroid dose formation has been justified in order to account for systematic errors. The main statements of the modified semiempirical model of thyroid dose formation have been described. The problem regarding possible production of fresh fission products (including short-lived radioiodines) at the time of the explosion of the Chernobyl reactor is presented. The main materials related to presentation of the results of our investigations on thyroid dose reconstruction in Belarus were in the literature, for example, Refs. [1–4]. This is the reason for which they are described here in a shortened view. The main attention is paid to the questions, which are actual for the time being, and those questions are likely to be actual in the future. Because of their importance those questions are being discussed in the framework of BelAm and UkrAm thyroid cohort projects as well as of the other projects.

Keywords: Chernobyl accident; Belarus; Thyroid dose; Calculation models; Fresh fission products

1. The main stages of the work conducted on thyroid dose reconstruction

1. Collection of more than 250,000 results of direct thyroid measurements for the Belarusian residents in Gomel and Mogilev Oblasts and in Minsk city.
2. Organization and implementation of personal interviews of approximately 150,000 residents living in the most contaminated areas in Gomel and Mogilev Oblasts.

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PII: S0531-5131(01)00619-7

3. Verification and systematization of the results of direct thyroid measurements and putting them into computer data bank.
4. Determination of the systematic errors in the results of direct thyroid measurements.
5. Thyroid dose calculation for about 130,000 inhabitants of Belarus.
6. Determination of average thyroid doses for the populations living in 900 settlements in Belarus.
7. Passportization of the settlements according to levels of thyroid exposure to the residents.
8. Comparison of average thyroid doses for the residents in the settlement with average ground deposition densities of ^{131}I and ^{137}Cs in the vicinities of a given settlement.
9. Development of the semiempirical model of thyroid dose formation.
10. Account for contribution from short-lived radioiodines ($^{132}I-^{135}I$) to thyroid exposure.

2. The main results of thyroid dose reconstruction

Calculation of individual thyroid dose for the resident in the settlement is carried out using one of the three possible methods depending upon whether the residents in that settlement have the results of direct thyroid measurements. So, the estimates of thyroid dose have been divided into three classes: Class 1 ("measured" doses), Class 2 (doses "derived by affinity" so-called "passport" doses), and Class 3 ("empirically derived" doses). The higher the Class number, the more uncertainty in the dose estimate.

Class 1 contains estimates of dose derived from the results of direct thyroid measurements.

Class 2 contains estimates of dose calculated on the basis of the passport of the settlement.

Class 3 contains estimates of dose reconstructed by the use of the semiempirical model.

Table 1 presents average thyroid dose estimates for the three age groups of the residents living in areas of Belarus. The presented estimates of thyroid dose were calculated as of the beginning of 1996. The maximum value of average dose = 4.7 Gy was realized for age-group of 0–6 years in the 30-km zone in Khoiniki raion in Gomel region.

It is important to stress that all the estimates of thyroid dose in Table 1 were calculated assuming a non-nuclear nature of the Chernobyl accident. It means that in such case thyroid dose for the residents was mainly formed due to exposure from ^{131}I taking into account the ratios of short-lived radioiodines ($^{132}I-^{135}I$) to ^{131}I in the reactor at the time of the steam (hydrogen) explosion. Reality of that assumption is considered in the final section of the paper.

3. Account for systematic errors under calculation of Class 1 individual thyroid dose estimates

This problem is especially actual for Belarus because, during in vivo monitoring of ^{131}I-thyroid content and reporting the results a lot of mistakes occurred. It resulted to the fact that

Table 1
Average thyroid dose (mGy) for the three age-group residents in areas of Belarus [4]

Area	Age-group			Total
	0–6 years	7–17 years	Adults	
Minsk city[a]	80	29	18	27
Minsk region	14	7.0	4.7	6.1
Total in Minsk region	48	180	11	17
Gomel city[a]	461	160	78	140
Evacuated villages (before 5 May 1986) in Bragin, Khoiniki and Narovlya districts[a]	2800	1400	990	1200
Non-evacuated villages (before 5 May 1986) in Bragin, Khoiniki and Narovlya districts[a]	1200	550	330	460
Other areas of Gomel region with sufficient number of Class 1 doses[a]	450	250	120	180
Remaining areas of Gomel region where the thyroid measurements were not conducted	650	240	170	230
Total in Gomel region	610	240	150	220
Mogilev city[a]	81	31	20	29
Five districts of Mogilev region: Slavgorod, Klimovichi, Krasnopolye, Kostukovichi, Chericov[a]	300	140	96	120
Remaining districts of Mogilev region	83	30	23	31
Total in Mogilev region	100	41	31	40
Total in Brest region	99	36	26	37
Total in Vitebsk region	6.0	2.8	2.0	2.6
Total in Grodno region	23	8.3	5.8	8.1
Total in Republic	150	58	38	53

[a] Average doses were calculated on the basis of the direct thyroid measurements.

the values of average exposure rate near thyroid, P_{nj}, calculated for each set of sufficient number (n) of measurements of the residents from the same settlement (j) measured at different places and times to a common date were very different (up to factor of 5 and even more).

Systematic errors due to the above reasons can be accounted for by using the following method. Among all the values of average exposure rate near thyroid, P_{nj}, calculated for different sets of direct thyroid measurements the value is chosen, P_{nj0}, which is the most close to the corresponding value, P_{Mj}, which is calculated by the use of the most adequate model of thyroid dose formation. In our opinion, the modified semiempirical model of thyroid dose formation should be used for that purpose. Then, all the other values of average exposure rate near thyroid, P_{nj}, which are located outside the range of variation of P_{nj} near P_{nj0}, should be corrected by multiplying the correction coefficient in order to reach the closest border of the range considered (left border or right border).

4. Calculation of Class 2 individual thyroid dose estimates ("passport" doses)

Average thyroid dose for the adults, D_j, in the settlement considered (j) calculated using Class 1 doses, is the basis for the calculation of "passport" doses, D_{ij}, for the residents in that settlement. In order to calculate D_{ij} for the residents of any age, the dose D_j is multiplied by the age-dependent coefficient K_{ij}, whose value is taken from the table presented in Ref. [5] taking into account the individual rate of fresh milk consumption locally produced including zero milk consumption rate. In the latter case dose to thyroid D_{ij} is due to inhalation intake of radioiodines. If there is no information regarding individual rate of milk consumption, then the value of K_{ij} is taken which is typical for the given age of the residents. The passports developed for approximately 900 settlements in Belarus allow to calculate individual thyroid doses for about 2,700,000 residents including the inhabitants of Minsk City.

5. Calculation of individual thyroid dose estimates on the basis of the modified semiempirical model (Class 3 doses)

Taking into account the results of comparison of average thyroid dose, D_{mj}, (so-called "measured" average doses, index "m") calculated on the basis of Class 1 doses and radionuclide ground deposition density, q_j, in the vicinities of the corresponding settlement considered (j), as well as analytical analysis [6], it was shown that the average thyroid dose depended upon the type of ^{131}I deposition (dry—index "d", wet—index "w", and combined—index "c"). In general case the average thyroid dose for the residents who were not measured should be estimated according to the following four equations:

$$D_{dj} = C_d \times q_{dj}; \qquad D_{Mj} = B \times q_{Mj} \qquad D_{cj} = C_c \times q_{dj} + B \times q_{cj}; \tag{1}$$

$$D_{cjx} = C \times q_x + B \times q_{cj}; \tag{2}$$

where

$$C_d = B \times (1 + \mu_1 \times \mu_2)/(1 + \mu_2); \quad C_c = B \times \mu_2 \times (\mu_1 - 1)/(f \times (1 + \mu_2)); \quad B = F \times S_s; \quad C = C_c \times q_{dj}/q_j \tag{3}$$

$$\mu_1 = S_g/S_s; \qquad \mu_2 = q_{gd}/q_{sd}; \qquad f = q_{gd}/q_{gc}; \tag{4}$$

where, S_g—effective surface, from which ^{131}I goes to grazing animal with pasture grass (index "g"), m^2; S_s—reduced surface, from which ^{131}I goes to grazing animal with soil (index "s"), m^2; q_{gd}—dry deposition onto grass, Bq m^{-2}; q_{sd}—dry deposition onto soil, Bq m^{-2}; q_{gc}—combine deposition onto grass, Bq m^{-2}; F—age-dependent dose factor, Gy Bq^{-1}; q_x—ground deposition density of ^{131}I on average over the delineated territory (x), Bq m^{-2}.

Eq. (2) should be used if it is impossible to delineate the territories with only dry deposition in the vicinities of the settlement considered (j) or in the vicinities of the neighboring settlements. The values of the generalized coefficients C_d, C_c, B, and C for different areas are determined by analyzing the dependence of the values of D_{mj} as a function of the measurable parameters q_{dj}, q_{Mj}, q_{cj}, and q_x or according to Eq. (3) if it is possible. Different lifestyle and dietary habits of the residents living in different areas during the period of thyroid dose formation are taken into account by insertion addition multiplied coefficient into Eqs. (1) and (2).

It is necessary to take into account that deposition of large radioactive particles can be considered as wet deposition with respect to deposition onto grass and soil.

In the case of the use of ground deposition densities of ^{137}Cs, then the values of q_{dj}(I), q_{Mj}(I), q_{cj}(I), and q_x(I) for ^{131}I in Eqs. (1) and (2) are replaced by the corresponding values for ^{137}Cs:

$$q_{dj}(\mathrm{I}) = R_{dj} \times q_{dj}(\mathrm{Cs}), \quad q_{Mj}(\mathrm{I}) = R_{Mj} \times q_{Mj}(\mathrm{Cs}), \quad q_{cj}(\mathrm{I}) = R_{cj} \times q_{cj}(\mathrm{Cs}), \quad q_x(\mathrm{I}) = R_x \times q_x(\mathrm{Cs}) \tag{5}$$

In order to determine the type of radionuclide deposition one can use:

- the data received from meteorological stations;
- the results of the determination of ^{137}Cs ground deposition density with identification of spots, which are characterized by sharp increase in the values of q, as a rule, it evidences about wet deposition;
- "effect of bent birch tree" [7], showing that exposure rate, A_1, on the side of the bent birch tree is substantially higher than that, A_2, on the opposite side of the tree in the case of wet radioactive fallout, while in the case of dry deposition (including deposition of large radioactive particles) such effect is absent.

In order to identify the deposition of large radioactive particles, special investigations need to be carried out.

6. The problem regarding possible contribution to thyroid exposure for the Belarusian people of short-lived radioiodines (^{132}I–^{135}I) freshly produced

Since 1991 in some publications, for example, Refs. [8,9], the information pointing out to the nuclear nature of the Chernobyl accident (regarding the way of energy release) has appeared. No fuel was discovered in the reactor core shaft. No fuel-containing masses, which could have reached underground water, were realized. Small amount of fuel was found in the reactor of the fourth block after the explosion of the reactor core, which resulted in its lifting at a height of about 17–18 m due to reactive flight.

Many "anomalous" (from widely accepted point of view of non-nuclear scenario of the accident) facts and results of the study of radionuclide ratios in fallout and in air above the reactor [10] (in particular, many values of the ratio of ^{134}Cs to ^{137}Cs exceeding the ratio of those radionuclides in the reactor at the time of the accident) were reported. In such case, one cannot exclude substantial production of fresh fission products in a local area of reactor core and their release to the Belarusian side according to wind direction. Then (if the nuclear scenario of the accident is correct), we can expect more substantial intake of short-lived radioiodines by the residents living in downwind directions and corresponding increase of thyroid morbidity.

Because of the importance of the problems mentioned above we should study it more carefully. Multi-factor analysis of all the available materials should be carried out. The quality of the results of the investigations aimed at the study of the dependence "dose-effect" depends upon the resolving of the problem mentioned above.

References

[1] Y.I. Gavrilin, V.T. Khrouch, S.M. Shinkarev, Internal thyroid exposure of the residents in several contaminated areas of Belarus, Med. Radiol. 6 (1993) 15–20 (in Russian).

[2] Y.I. Gavrilin, V.T. Khrouch, S.M. Shinkarev, N. Krysenko, A. Skryabin, A. Bouville, L. Anspaugh, Chernobyl accident: reconstruction of thyroid dose for inhabitants of the Republic of Belarus, Health Phys. 76 (2) (1999) 105–119.

[3] Y.I. Gavrilin, V.T. Khrouch, S.M. Shinkarev, Achievements, problems, and the ways of resolving them for internal thyroid dose reconstruction as a result of the Chernobyl accident, in: M. Hoshi, J. Takada, R. Kim, Y. Nitta (Eds.), Proceedings of the Second Hiroshima International Symposium "Effects of Low-level Radiation for Residents Near Semipalatinsk Nuclear Test Site", Hiroshima, Japan, 23–25 July, 1996, Hiroshima University, Hiroshima, 1996, pp. 85–100.

[4] V. Minenko, Y. Gavrilin, S. Shinkarev, V. Khrouch, E. Shemyakina, V. Drozdovitch, A. Bouville, P. Voilleque, N. Luckyanov, Chernobyl accident: assessment of the collective thyroid dose for the Belarusian population, Proceedings of the 10th International Congress of the International Radiation Protection Association, Hiroshima, Japan, 14–19 May 2000, index P-11-263.

[5] Y. Gavrilin, V. Khrouch, S. Shinkarev, V. Stepanenko, Assessment of internal thyroid dose from ^{131}I on the basis of the results of measurements of ^{129}I in environments. Methodical directions. MU 2.6.1.082-96 State Sanitary-Epidemiology Supervision. Russia, Moscow, 1996, 26 pp. (in Russian).

[6] Y. Gavrilin, V. Khrouch, S. Shinkarev, Validation of semi-empirical model of thyroid dose estimation and delineation of territories (x) under assessment of average thyroid doses for adult rural residents, Bull. Public Inf. Cent. At. Energy, Moscow 11 (1999) 33–42 (in Russian).

[7] V.F. Stepanenko, Y.I. Gavrilin, V.P. Snykov, V.E. Shevchuk, H.Y. Goeksu, P.G. Voilleque, M.Y. Orlov, Elevated exposure rates under inclined bent birch trees indicate the occurrence of rainfall during radioactive fallout from Chernobyl, Health Phys., submitted for publication.

[8] K.P. Checherov, Present-day understanding of the reasons and the processes of the accident at the 4th block of the Chernobyl NPP, Materials of the International Scientific–Practical Conferences Devoted to the 10th and 12th years after the Chernobyl Accident (April 18, 1996 and April 24, 1998). Abstracts of the Reports. Moscow, 4th branch of Voenizdat, 1998, pp. 111–116 (in Russian).

[9] A.N. Kiselev, K.P. Checherov, The process of destruction of the reactor at the 4th block of the Chernobyl NPP, Bull. Public Inf. At. Energy, Moscow, (in press) (in Russian).

[10] Y.I. Gavrilin, The consequences of the two scenario of the accident, Bull. Public Inf. At. Energy, Moscow 10 (2001) 20–25 and 11 (2001) 40–47 (in Russian).

International Congress Series 1234 (2002) 307–319

Distribution of childhood thyroid dose among cohort members for epidemiological health study in the Bryansk region

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Abstract

With the aim of carrying out a long-term medical follow-up with radiation dose reconstruction, a cohort of subjects was selected among inhabitants of the most contaminated area in Russia following the Chernobyl accident (the western districts of Bryansk region). The cohort is comprised of 1065 subjects who were under 10 years old at the time of the accident. Most of them were examined on health status in the Chernobyl Sasakawa Health and Medical Cooperation Project. Since the main findings of studies in the project were thyroid abnormalities, selection of subjects was conducted on the basis of the plausible estimates of radiation dose to the thyroid. To estimate thyroid doses, the data from direct measurements of ^{131}I in the thyroid and questionnaire data on individual dietary habits in May 1986 were used. Reasonable approximations were applied to reconstruct individual doses from available data, including doses for those persons who had not been measured for thyroidal radioiodine. The distribution of internal radiation dose to the thyroid among cohort members was obtained. The individual doses to particular subjects are estimated with inevitably essential degree of uncertainty. However, the distribution of subjects into wide dose intervals, from under 200 mGy to over 2 Gy, seems to be an acceptable approach for cohort study in radiation epidemiology. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Chernobyl; Dosimetry; Iodine-131; Thyroid

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PII: S0531-5131(01)00620-3

1. Introduction

Radioactive contamination of large areas following the Chernobyl accident stimulated the undertaking of epidemiological studies of possible health effects of low radiation doses. The important task in radiation epidemiology studies is the evaluation of individual radiation doses to the members of population samples under consideration. The joint research project conducted by Sasakawa Memorial Health Foundation (Japan) and the Research Institute of Radiation Hygiene (RIRH, Russia) was launched to assign individual doses to the children in the Russian Federation under 10 years old at the time of the accident who were subjected to health screening within the framework of the Chernobyl Sasakawa Health and Medical Cooperation Project (CSHMCP). It has been agreed to establish a cohort of about 1000 subjects selected in line with supposed individual dose distribution appropriate to the purpose of investigating health effects by long-term medical follow-up. Since the main findings of studies in the CSHMCP were thyroid abnormalities [1], selection of cohort members was conducted on the basis of the plausible estimates of thyroid dose. The paper describes dosimetry and questionnaire data used in the study, as well as the approaches accepted to estimate individual doses and to derive distribution of cohort subjects among intervals of thyroid dose.

2. Materials and methods

2.1. Selection of cohort members

The measurement of radioiodine in man is of primary importance for the estimates of individual dose. However, only a small percentage of children examined in CSHMCP were found to be measured on ^{131}I in the thyroid properly and in due time. Unmeasured subjects were selected on the basis of availability of environmental and questionnaire data that may prove useful for the estimates of thyroid dose. On the other hand, some persons were included in the cohort who had been measured for thyroidal radioiodine, but who had not been included before in the Chernobyl Sasakawa investigation. The procedure for cohort selection was described in more detail earlier [2]. Finally, the cohort is comprised of 1065 subjects under 10 years old (at the time of the accident) who were residing in the western districts of the Bryansk region, i.e., in the territory of the Russian Federation most affected by radioactive contamination following the Chernobyl accident. The level of contamination in terms of ^{137}Cs ground-deposition density ranges from 170 kBq m^{-2} to 2.8 MBq m^{-2} in the settlements where cohort members were residing.

2.2. Direct thyroid measurements

The most part of timely and qualified thyroid measurements in Russia following the Chernobyl accident were carried out by the Institute of Medical Radiology (now the Medical Radiological Research Center of the Russian Academy of Medical Sciences) in the Kaluga region where the level of radioactive contamination was not so high as in the western districts of the Bryansk region [3]. Most measurements recorded in the Bryansk region were carried out by inexperienced (in dosimetry) personnel from the local health service. These measurements are of use in thyroid dose reconstruction studies with laborious work to verify data in view of incomplete records and/or problems of retrospective calibration of measuring devices [4,5]. For consideration in the present study, only reliable data from the measurements performed by the staff of RIRH in May–June 1986 are used.

There were two types of devices used in RIRH for measurement of radioiodine in the thyroid: stationary spectrometry whole-body counter (WBC) and gamma radiometry devices. Most measurements were made with portable or transportable units: gamma and X-radiation dosimeter DRG3-02 (Russia) with scintillation plastic detector containing dispersed luminophor ZnS(Ag); gamma radiometer SRP-68-01 (Russia) with scintillation crystal NaI(Tl) of a 30-mm diameter by 25 mm thick; and one-channel scintillation spectrometry radiometer VA-M-141 (RFT, East Germany). The most widely used, especially in field conditions, was radiometer SRP-68-01 in view of its accessibility, compactness and portability.

Calibration of all devices was performed by means of thyroid phantom with certified activity of ^{131}I. The paraffin phantom of the human neck contained a plastic ball filled with the standardized water solution of ^{131}I. Applying non-spectrometric devices, calculation of ^{131}I activity in the thyroid from measurement data was carried out taking account of the contribution of incorporated radiocesium into registered gamma radiation from the neck. To evaluate this contribution and to derive correction factors, special research was performed by analysis of WBC spectrometry data for 253 persons of various age on the body content of incorporated radionuclides, including ^{131}I, ^{134}Cs and ^{137}Cs. The values of correction factor were derived for various ages of individuals and for various times of measurement.

There are two sets of measurements taken into consideration in this study: examination of people who arrived in Leningrad (St. Petersburg) from contaminated areas and examination of the local population in the settlement situated in the Bryansk region. Soon after the Chernobyl accident, the Research Institute of Radiation Hygiene, local administration and health services organized a special sanitary unit to check the surface and internal radioactive contamination of people who were arriving in Leningrad from the regions of Russia, Belarus and Ukraine affected by exposure to radiation following the accident. From the total number of 2676 persons examined for internal radioactivity, 310 residents from seven of the most contaminated districts of the Bryansk region were found who had been measured for ^{131}I content in the thyroid from May 17 to June 15, 1986; among them, 146 children 0–10 years old. Data from later measurements are not taken into consideration because of their insignificance in view of radioactive decay of ^{131}I and excretion of radioiodine from the body. The contents of ^{131}I in the thyroid of children of different age derived from the measurements of 146 subjects are shown in Fig. 1. The presented data are extrapolated to a common date (May 22) for comparability of data derived from measurements performed at different days. The extrapolation was made by exponential factor accounting for age-dependent half-time of ^{131}I in the thyroid.

During the radiological monitoring in the most contaminated territory of the Bryansk region carried out by RIRH, residents of the settlement Mirny (^{137}Cs contamination level of 1.3 MBq m^{-2}) were examined on the content of radioiodine in the thyroid. Measure-

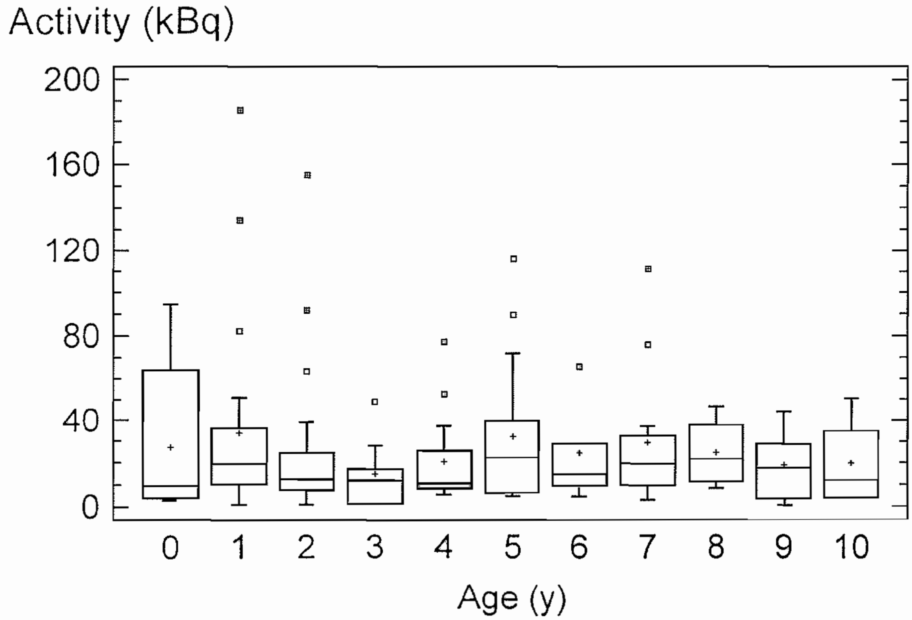

Fig. 1. The box-and-whisker plots of ^{131}I activity in the thyroid of children from the Bryansk region measured in Leningrad (St. Petersburg) from May 17 to June 15, 1986. Measurement data are extrapolated to the reference date of May 22. The bottom and top of each box represents 25% and 75% of the data, while the line through the middle is the median. The points outside whiskers are those which lie more than 1.5 times the interquartile range.

ments were made at May 22, 1986 with portable radiometer SRP-68-01. Measurement data corrected for contribution of radiocesium are presented in Fig. 2 for 283 children who were residing in Mirny.

2.3. Questionnaire data

It is seen in Fig. 2 that even in a single settlement, the distribution of individual thyroid burdens of ^{131}I measured at the same time and in the same age group is very wide. Sources of variability in the measured values of ^{131}I activity in the thyroid are not related to instrumental errors but to environmental and lifestyle factors. This variability, first of all, resulted from individual dietary differences including food habits and the perception that a person or family had with respect to radiation risk and recommended countermeasures. Locally produced milk from cows grazing on contaminated pastures usually provided the main contribution into ^{131}I intake via food. Therefore, information on food habits, mainly on consumption of milk in May 1986 is useful both to interpret the measurement data and to ascribe a dose value to those subjects who had not been measured on ^{131}I in the thyroid.

For the purpose of this study, available information on individual dietary behavior was analyzed on the basis of primary records from mass examination of people in the western districts of the Bryansk region carried out by RIRH after the Chernobyl accident. During February–April and July 1987, along with the whole-body measurements of radiocesium, the inhabitants of the Bryansk region were interviewed with respect to their lifestyle and

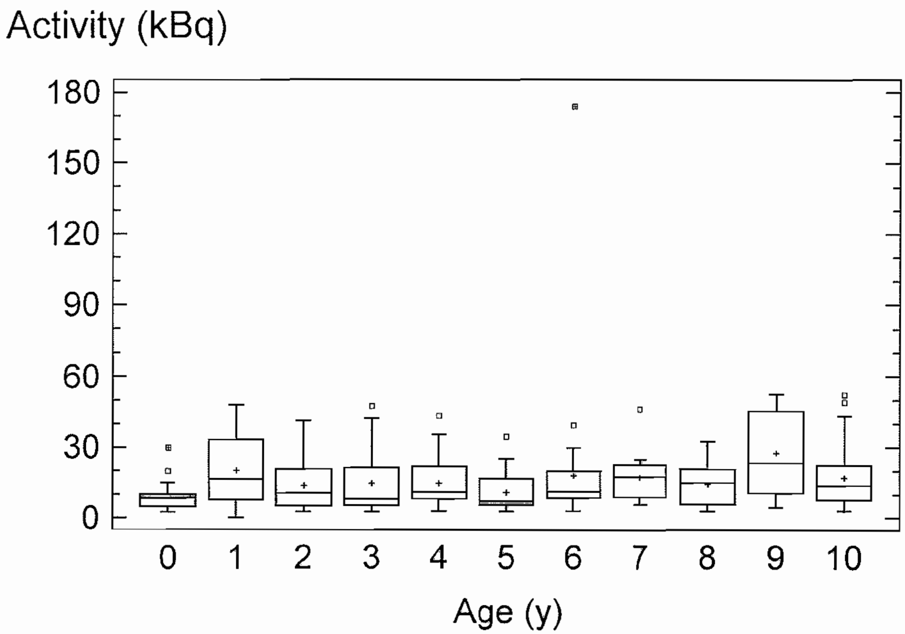

Fig. 2. The box-and-whisker plots of ^{131}I activity in the thyroid of children in Mirny (Bryansk region), May 22, 1986. See Fig. 1 for details of the plot.

diet at the early post-accident period. Questions were asked about consumption of local food products, the daily amount and sources of consumed milk, the date of taking advice to stop consumption of locally produced milk, dates of temporal relocation in 1986. The concentration levels of ^{131}I in milk were in excess of temporary permissible levels established by the State Sanitary Authorities, and a ban on local milk consumption in the contaminated territories was launched. However, people stopped consumption of locally produced milk at various times. Analysis of questionnaire records for 11 080 examinees who were 0–10 years of age at the time of the accident revealed 4988 replies related to the date of discontinuation of local milk consumption. The median of dates distribution was 16 May, 1986, i.e., T=18 days after the start of radioactive contamination of the territory (28 April, 1986 for the western districts of the Bryansk region). However, this value was less for children in the most contaminated settlements, where countermeasures had been initiated earlier and more intensively. As an example, Fig. 3 shows the distribution of duration of locally produced milk consumption in the village Yalovka (^{137}Cs contamination of 2.8 MBq m^{-2}), where the median value of T was 12 days.

2.4. Individual dose for subjects measured on ^{131}I in the thyroid

The pasture–cow–milk pathway is assumed to be the dominating contributor of ^{131}I into the human body, and the model of radioiodine content in the thyroid was approximated in the present study by the constant intake rate during T days after the

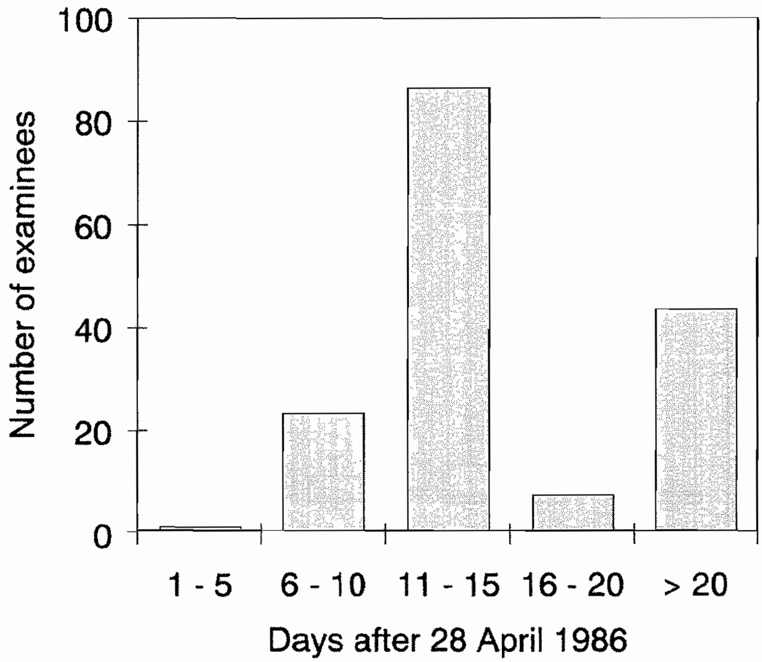

Fig. 3. The length of time during which contaminated milk was consumed by children under 10 years old in the village Yalovka.

beginning of radioactive deposition on the territory and no further intake after T. The value of T was taken as 20 days in the absence of countermeasures, or $T<20$ days in the case of earlier interruption of ^{131}I intake by the following actions: departure of the individual from contaminated area, stopping consumption of contaminated milk (see Fig. 3), iodine prophylaxis (intake of stable iodine preparations effective in blocking the uptake of ^{131}I by the thyroid). This simplified approach yields practically the same results in dose reconstruction as the sophisticated models describing processes of ^{131}I migration from initial deposition on the territory to the human thyroid after the Chernobyl accident.

In line with the above, the calculation of individual dose (D_{ind}, mGy) for those cohort members who had been measured for iodine-131 in the thyroid was carried out by the following equation:

$$D_{\text{ind}} = A_t k_a \frac{\lambda_a T_{\text{ind}} e^{\lambda_a (t - T_{\text{ind}})}}{1 - e^{-\lambda_a T_{\text{ind}}}}, \qquad (1)$$

where: A_t, kBq—the content of ^{131}I in the thyroid at time t; t, days—the time elapsed from 28 April, 1986 to the date of measurement; T_{ind}, days—individual value of T (see above), counted from 28 April, 1986; $_a$, day^{-1}—age-dependent effective constant of ^{131}I excretion from the thyroid; k_a, mGy kBq^{-1}—age-dependent absorbed dose per unit intake of ^{131}I in the thyroid.

Eq. (1) is valid for $t > T_{\rm ind}$ (corresponding to the measurements under consideration). Values of ${}_a$ and k_a were taken from ICRP Publication 67 [6] and updated from the latest paper on this topic [7]. Values of $T_{\rm ind}$ were derived from available questionnaire data.

2.5. Derivation of thyroid dose for unmeasured subjects

Various methods were considered to estimate thyroid doses for the residents of contaminated settlements where no measurement data are available [8,9]. The methods suggested a correlation of reference thyroid dose (the mean thyroid dose for some age groups) with various environmental and behavioral factors in the first weeks after the accident in the place where people resided. The environmental factors explored were the ground-deposition density of iodine-131 (S_{131}) or cesium-137 (S_{137}), the kerma rate in air (p), the concentration of ^{131}I in locally produced cows' milk ($q_{\rm m}$), as well as the radiocesium body burden measured during the first months after the accident ($A_{\rm Cs}$). The behavioral factor under consideration was the consumption of cows' milk: daily amount in diet and dates when the consumption of contaminated milk was stopped.

For the purpose of the present study, the analysis of various methods for dose reconstruction was carried out. Special attention was paid to the availability and reliability of numerical values of environmental and behavioral parameters involved into the suggested correlation. This analysis resulted in the conclusion that the most appropriate general approach might be a relationship between ^{137}Cs contamination of the territory (S_{137}, kBq m^{-2}) and the representative thyroid dose in specified settlement ($D_{\rm th}$, mGy). Information on ^{137}Cs contamination is available for all settlements with $S_{137} > 37$ kBq m^{-2} [10], while the data for other considered environmental factors are scarce and not so reliable as for S_{137}.

Balonov et al. [11] found that the thyroid dose correlated with S_{137} is better than with other factors (p, $q_{\rm m}$, $A_{\rm Cs}$) and proposed that the mean dose for children 3–6 years old might be evaluated as:

$$D_{\rm th} = 0.76 \cdot S_{137}. \qquad (2)$$

Gavrilin et al. [12] proposed more universal formulae where the ratio of the ^{131}I to ^{137}Cs ground-deposition was taken into account. However, this ratio is practically constant for the territory under consideration (western districts of Bryansk region) [10]. Considering various distances from Chernobyl, the regression equation was formulated applying to the reference age of 3 years [13]:

$$D_{\rm th} = g + h \cdot S_{137}, \qquad (3)$$

where parameters g and h are different for the settlements with S_{137} above 400 kBq m^{-2} (374 and 0.44) and for those with lower contamination (105 and 0.95 for Bryansk region).

In the present study, in view of most cohort subjects under consideration (96%) were residing in the settlements with $S_{137} > 400$ kBq m^{-2} and in account of age-dependence of dose factor (k_a), a satisfactory approximation to the above relationships is found for 3-year-old children:

$$D_{\mathrm{th}} = 0.94 \cdot S_{137}. \tag{4}$$

Individualization of thyroid dose is based on the assumption that the main contribution to intake of radioiodine was delivered by consumption of milk, but with account of some contribution from inhalation and consumption of other food items, mainly leafy vegetables. Time integrated intake via milk was presented by the product of consumption rate (V, l day^{-1}) and effective duration of consumption of contaminated milk (T, day). This approach for the individual dose was expressed by the following equation [14]:

$$D_{\mathrm{ind}} = D_{\mathrm{th}}\left[f + (1-f)\frac{V_{\mathrm{ind}}T_{\mathrm{ind}}}{VT}\right], \tag{5}$$

where D_{th}, V and T are the representative values for the settlement and age group, and D_{ind}, V_{ind}, T_{ind} are the individual values. It was assumed that the fraction of non-milk intake was f=0.2 [14].

Based on questionnaire data, a reasonable simplification is introduced in the present study by assumption that the mean value of consumption rate was V=0.5 l day^{-1} and T=20 days where countermeasures were not undertaken. Substitution of Eq. (4) for D_{th} results in the following approach to derive the individual dose for unmeasured cohort subjects:

$$D_{\mathrm{ind}} = 0.94 \cdot S_{137}\frac{k_a}{k_3}[f + 0.1(1-f)V_{\mathrm{ind}}T_{\mathrm{ind}}], \tag{6}$$

where k_3 and k_a are the dose coefficients for a 3-year-old infant and for a subject of a years.

Inhalation rate and consumption of green vegetables are less for younger children. For this reason, the non-milk fraction of dose (f) is assumed to be age-dependent for a<11 years:

$$f = 0.05 + 0.005\ a. \tag{7}$$

3. Results and discussion

Individual dose was calculated according to Eq. (1) for cohort members measured for ^{131}I in the thyroid and to Eq. (6) for other subjects. Distribution of subjects among the intervals of thyroid doses, from <0.2 to >2 Gy is shown in Fig. 4. This distribution is not representative for population of the territory under consideration, because subjects unmeasured for thyroidal radioiodine were intentionally selected from those examined in the Chernobyl Sasakawa Project for whom the dose might be individualized by available questionnaire data.

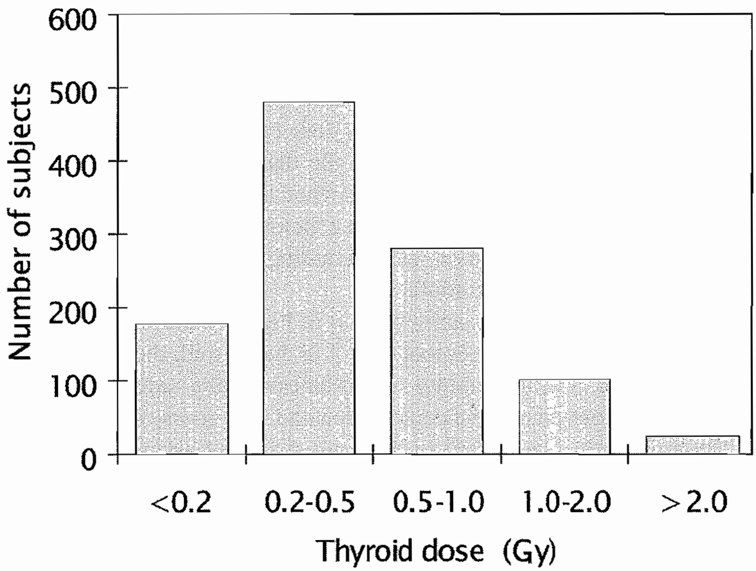

Fig. 4. The distribution of cohort subjects among the intervals of thyroid dose.

A set of assumptions was taken for approach to individual dose with Eqs. (1) and (6) using incomplete or partially relevant data. Therefore, an actual thyroid dose might be significantly different from D_{ind} ascribed to a specified person as a result of dose reconstruction based on the available data. It is hardly possible to make a correct evaluation of uncertainty in estimation of individual dose. Nevertheless, the degree of uncertainty should be realized by consideration of main features of dose reconstruction. The following discussion considers this matter.

Usually, individuals were measured for ^{131}I in the thyroid only once. There is an inevitable uncertainty in calculation of the individual dose from a single measurement, because we have to know the dynamics of ^{131}I content in the gland both before and after the measurement. An analytical research was carried out in the present study to obtain a range of uncertainty in common case when the measured ^{131}I activity in the thyroid, the date of measurement and the age of examined person are known. Three modes of intake of ^{131}I into the human body were taken into account: inhalation, consumption of leafy vegetables and consumption of milk. An instantaneous inhalation intake, one-exponent model of ^{131}I concentration in greens after their surface contamination and two-exponent model of ^{131}I concentration in cows' milk following the deposition of radionuclide on pasture were considered with the wide variation of numerical values of parameters derived from published data and reviews [15–17]. For different combinations of intake modes, models and parameters, as well as taking account of the effect of countermeasures (e.g., discontinuation of consumption of contaminated food or iodine prophylaxis), the ratio between the absorbed thyroid dose and the unit of ^{131}I activity in the thyroid (dose–activity ratio) was calculated as a function of time of measurement after the start of contamination.

The details of this analytical research will be published elsewhere. The results of calculations are shown in Fig. 5 applying to a 3-year-old infant. The column presented for each day of measurement extends from the lowest to highest value of dose–activity ratio. The length of columns represents uncertainty in dose calculation. This uncertainty varies with the day of measurement (t) counted from the date when deposition of ^{131}I on the territory was started. It is lowest at t=10–16 days when deviation from the geometric mean between the top and bottom of columns is within a factor of 1.5. The deviation exceeds 2.0 at $t>30$ days. The uncertainty decreases with increasing age, i.e., it is relatively higher for younger children and the lowest for adults.

The calculated range of the dose–activity ratio in Fig. 5 is related to the case when no information is available besides the content of ^{131}I in the thyroid, the date of measurement and the age of examinee. The uncertainty would be essentially reduced by available data and reasonable assumptions on relative contribution and time course of various pathways of ^{131}I intake. The milk path is suggested to be dominating, but assumption of the constant intake rate during T days (Section 2.4) means that inhalation and consumption of surface-contaminated foods, mainly green vegetables, would compensate an overestimation of milk contribution during exponential rise of ^{131}I concentration in cows' milk at the initial time after deposition. This model was used to derive Eq. (1), and corresponding values of dose–activity ratio are exemplified by the curve in Fig. 5 for a 3-year-old old infant and T=15 days.

In estimates of the individual dose for unmeasured subjects by Eq. (6), two points are delivering the main uncertainty additional to real variance of D_{th}/S_{137} ratio. The first one is insufficient reliability of V_{ind} and T_{ind} values derived from personal interviews. Most individuals do not remember these factors with accuracy. The second is the assumption

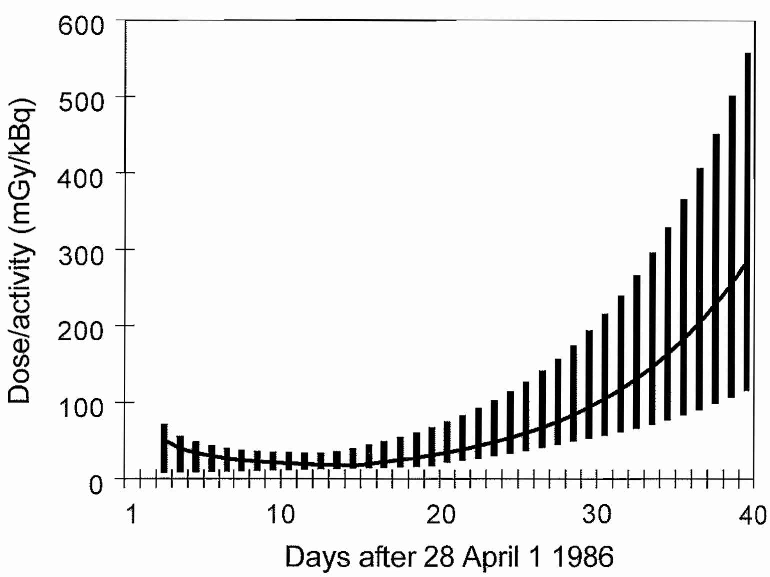

Fig. 5. The ratio of thyroid absorbed dose to the measured ^{131}I content in the thyroid of a 3-year-old infant.

that the concentration of ^{131}I in locally produced milk was the same for all subjects in the specified settlement. In real situations, the ^{131}I concentration in milk varied at the same time and in the same settlement as a result of non-uniform deposition of ^{131}I on pastures, the variability in the consumption rate of grass by different cows, the use of cultivated pastures and uncontaminated stored forage and other factors. Assumption was used for values of T in Eqs. (1) and (6) that milk-producing cows began to consume contaminated feed just after deposition of ^{131}I on pastures, while at some farms, graziery started some days after 28 April 1986 (for these cases, the dose is overestimated or T_{ind} should be counted from the date of the beginning of cows' pasture).

The values of D_{ind} estimated in the present study are the absorbed doses in the thyroid from incorporated ^{131}I. The contribution of short-lived radioiodines into internal dose is negligible in situations with the dominating milk path of intake [15]. More essential addition to the thyroid dose might be delivered by external radiation from the environment, as well as from incorporated radiocesium (^{134}Cs and ^{137}Cs). Taking into account Eq. (4) and generalized ratio between whole-body dose and S_{137} in the Bryansk region due to the Chernobyl accident [18], the average addition in terms of adsorbed dose would be 4–13% for children 1–10 years old. This addition might be much larger in particular case of low intake of contaminated milk and effective countermeasures. Furthermore, it should be noted that there are suggestions of essentially higher biological effect of external gamma radiation to the thyroid as compared to that of internal exposure of the gland from ^{131}I [19,20]. Due to relatively low individual variability of exposure to external radiation and the large number of individual measurements of radiocesium in the body, the whole-body dose from the Chernobyl accident has been better studied than the thyroid dose. Therefore, the external dose to the thyroid can be taken into account if further epidemiologic and dosimetric efforts would be closely coordinated. Depending on interpretation of the relative radiation effects from external and internal exposure of the thyroid, the estimates of externally received thyroid dose can be either added to internal dose component or retained in the epidemiological analysis file for analysis as an additional risk factor.

We can conclude from the above discussion that the individual thyroid doses to particular subjects are estimated with an inevitable essential degree of uncertainty. However, this uncertainty can be considered as acceptable for cohort study in radiation epidemiology, where the distribution of cohort subjects among sufficiently wide dose intervals is needed rather than ascribing precise numerical dose values to each member of the cohort. This kind of presentation is shown in Fig. 4. Actual doses for some cohort members assigned to the predetermined dose interval may fall into the neighboring or even farther interval, but an appropriate number of subjects in each dose interval should provide the statistical consistency of epidemiological analyses. Availability of ascribed individual dose for each cohort member permits us to reorganize dose intervals, as well as to group subjects on the basis of any specific health end point under investigation and to consider the mean dose for each group.

Acknowledgements

This work was performed under the joint project between Sasakawa Memorial Health Foundation and the Research Institute of Radiation Hygiene, St. Petersburg (RIRH). The authors acknowledge the contribution of I. Bronshtein and S. Sukalskaya (RIRH) into the measurements of radioiodine in the thyroid of children in May–June 1986.

References

[1] S. Yamashita, Y. Shibata (Eds.), Chernobyl: A Decade, International Congress Series No. 1156, Elsevier, Amsterdam, 1997.
[2] Y.O. Konstantinov, O.S. Moskalev, M. Hoshi, Y. Shibata, S. Yamashita, Reconstruction of radiation doses to population in the western districts of the Bryansk Region due to the Chernobyl accident: application to cohort study in radiation epidemiology, Effects of Low-Level Radiation for Residents Near Semipalatinsk Nuclear Test Site. Proceedings of the Second Hiroshima International Symposium, Daigaku Press, Hiroshima (1997) 19–29.
[3] A.F. Tsyb, V.F. Stepanenko, E.G. Matveenko, V.A. Pitkevich, E.A. Ispenkov, V.N. Omelchenko, S.Y. Leshakov, Structure and levels of thyroid irradiation in population of contaminated areas of Kaluga region, Radiation and Risk 3 (1994) 129–135 (in Russian).
[4] I.A. Zvonova, M.I. Balonov, A.A. Bratilova, G.E. Baleva, S.A. Gridasova, M.A. Mitrokhin, V.P. Sazhneva, Thyroid dose estimation in the inhabitants of Bryamsk, Tula and Orel regions based on results of radiometry measurements in 1986, Radiation and Risk 10 (1997) 95–116 (in Russian).
[5] V.K. Ivanov, A.F. Tsyb, V.A. Pitkevich, M.A. Maksyutov, E.G. Marveenko, I.K. Khvostunov, E.M. Rastopchin, V.S. Sorokin, S.I. Ivanov, S.Y. Leshakov, V.I. Shiryaev, M.P. Borovikova, V.A. Efendiev, B.I. Kvitko, Y. Shibata, S. Yamashita, M. Hoshi, Selection of the cohort for long-term clinical follow-up and assessment of radiation risk for thyroid diseases under the joint medical research project conducted by Sasakawa Memorial Health Foundation and MRRC of RAMS, in: S. Yamashita, Y. Shibata (Eds.), Chernobyl: A Decade, International Congress Series No. 1156, Elsevier, Amsterdam, 1997, pp. 151–167.
[6] International Commission on Radiological Protection, Age-dependent doses to members of the public from intake of radionuclides: Part 2. Ingestion dose coefficients, ICRP Publication 67, Annals of the ICRP, vol. 23 (3/4), Pergamon Press, Oxford, 1993.
[7] B. Zanzonico, Age-dependent thyroid absorbed doses for radiobiologically significant radioisotopes of iodine, Health Physics 78 (1) (2000) 60–67.
[8] USSR Ministry of Public Health, Assessment of absorbed dose in the thyroid from radioiodine to people exposed due to the Chernobyl NPP accident, Methodical Instructions, USSR Ministry of Public Health, Moscow, 1987 (in Russian).
[9] I.K. Bailiff, V. Stepanenko (Eds.), Retrospective Dosimetry and Dose Reconstruction, EUR 16540 EN, European Commission, Luxembourg, 1996.
[10] Medical Radiological Research Centre of RAMS, Contamination of Russian territories with radionuclides ^{137}Cs, ^{90}Sr, $^{239}Pu+^{240}Pu$, ^{131}I, Radiation and Risk 3 (supplement 1) (1993) 1993 (in Russian).
[11] M.I. Balonov, G.Y. Bruk, V.Y. Golikov, V.G. Erkin, I.A. Zvonova, V.I. Parkhomenko, V.N. Shutov, Exposure to the population in Russian Federation as a result of the Chernobyl accident, Radiation and Risk 7 (1996) 39–71 (in Russian).
[12] Y.I. Gavrilin, V.T. Khrouch, S.M. Shinkarev, N.A. Krysenko, A.M. Skryabin, A. Bouville, L.R. Anspaugh, Chernobyl accident: reconstruction of thyroid dose for inhabitants of the Republic of Belarus, Health Physics 76 (2) (1999) 105–119.
[13] I.A. Zvonova, M.I. Balonov, A.A. Bratilova, A.Y. Vlasov, V.A. Pitkevich, O.K. Vlasov, N.G. Shishkanov, Methodology of thyroid dose reconstruction for population of Russia after the Chernobyl accident, Proceedings of the 10th IRPA Congress, Hiroshima, 2000.
[14] N.F. Korelina, G.Y. Bruck, G.N. Kaidanovsky, Y.O. Konstantinov, N.V. Porozov, Control and interpretation of radiometric survey data for determination of internal exposure to the thyroid after the Chernobyl accident, in: Y.O. Konstantinov (Ed.), Proceeding of the Russian–Hungarian Seminar on Radiation Protection, Research Institute of Radiation Hygiene, St. Petersburg, 1992, pp. 30–34.
[15] L.A. Ilyin, G.V. Arkhangelskaya, Y.O. Konstantinov, I.A. Likhtarev, Radioiodine in the Problem of Radiation Safety, Atomizdat, Moscow, 1972 (in Russian). Springfields VA: USAEC translation TR536, 1974.

[16] L.A. Ilyin (Ed.), Guidance on Thyroid Dose Assessment for Man Due to His Radioiodine Intake, Energoatomizdat, Moscow, 1988 (in Russian).
[17] Y.O. Konstantinov, Ecological forecast to provide radiation protection in the event of a single deposition of iodine-131 on pasture, Radiation Hygiene, Research Institute of Radiation Hygiene, Leningrad, 1985, pp. 41–44 (in Russian).
[18] United Nations Scientific Committee on the Effects of Atomic Radiation, Sources and effects of ionizing radiation, Annex J: Exposures and Effects of the Chernobyl Accident, United Nations, New York, 2000.
[19] NCRP Report No. 80. Induction of thyroid cancer by ionizing radiation. Bethesda, MD, National Council on Radiation Protection and Measurement, 1985, 1–93.
[20] United Nations Scientific Committee on the Effects of Atomic Radiation, Sources and effects of ionizing radiation, UNSCEAR 1994 Report to the General Assembly, United Nations, New York, 1994.

International Congress Series 1234 (2002) 321–328

Re-evaluation of thyroid doses in Russia after the Chernobyl accident

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Abstract

Immediately after the Chernobyl accident, the team of Medical Radiological Research Center (MRRC) specialists carried out wide-scale measurements of iodine-131 content in the thyroid gland of 27 887 inhabitants of the Kaluga region. This initial information was presented only as official reports to governmental structures. Similar work was done by local specialists for 1441 inhabitants of the Bryansk region. The data of direct measurements provided us the basis for further individual thyroid dose estimations, where we exploited the developed model and personal interviews. This paper presents the results of updated dose evaluations, including the additional factors, such as dynamics of fallout and data on the pasture period. According to new estimations, the median of individual dose values in the Kaluga database (seven districts) vary from 30 mGy for children to 8 mGy for adults (geometric standard deviation of about 2.6). In the database of Bryansk (five raions), the median dose values are ranging from 140 mGy for children to 30 mGy for adults (geometric standard deviation of about 2.7). The obtained data were used for the validation of the semi-empirical model for thyroid dose reconstruction. This allowed the reconstruction of the mean doses for the settlements where I-131 measurements were not performed. The collective thyroid doses for the

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PII: S0531-5131(01)00621-5

Bryansk and Kaluga regions were estimated as 72600 and 3400 persons-Gy (for population of 1137100 and 213500 inhabitants).

Keywords: Chernobyl accident; I-131; Thyroid dose; Individual dosimetry

1. Introduction

Iodine-131 is the main factor of internal irradiation of the thyroid gland in the population that inhabited the contaminated Russian territories on April–May 1986 [1]. The thyroid dose estimations in contaminated settlements of the Kaluga and Bryansk regions started in May 1986, in order to provide information for the evaluation of the possible consequences of the Chernobyl accident [2]. The team of Medical Radiological Research Center, Russian Academy of Medical Sciences (MRRC RAMS) specialists carried out wide-scale measurements of iodine-131 content in the thyroid gland of 27887 inhabitants of the Kaluga region [3]. Initial data were reported only to governmental structures as official report. Similar work was done for 1441 inhabitants of the Bryansk region by local specialists. Now, these data became very important for medical care and epidemiological studies of the thyroid cancer cases following the Chernobyl accident.

Thyroid dose calculations in 1986 were based on the results of direct measurements of I-131 content in the thyroid and on the data of personal interviews, excluding data on prolonged fallout and the dates of the pasture period.

Our further thyroid dose re-evaluations were performed in 1996, taking into account the recently published data concerning the time dependence of fallout and the dates of the pasture period. The results of this re-evaluation were reported only to the Ministry of Public Health of Russia [4]. The paper presents the main results of the updated thyroid dose evaluations.

2. Material and methods

The measurements of iodine-131 content in the thyroid gland of 27887 inhabitants of the contaminated Kaluga region were performed by specialists of MRRC RAMS during the period from 18 to 30 May 1986 in seven raions [3]: Khvastovichskiy (102 kBq/m^2 of caesium-137 ground deposition density), Zhsizdrinskiy (129 kBq/m^2), Ulianovskiy (191 kBq/m^2), Lyudinovskiy (102 kBq/m^2), Kuibishevskiy (39 kBq/m^2), Duminicheskiy (75 kBq/m^2), and Kozelskiy (41 kBq/m^2). Because of the lack of special equipment, all thyroid measurements were done by means of very simple instruments with analogue output in exposure rates: SRP-68-01 with NaI(Tl) scintillation detectors without collimator. As a rule, two measurements for each person were performed: first, close to the thyroid gland, and second, close to the abdomen area (near the liver). The second measurement was selected in order to evaluate the caesium-137 input readings from the thyroid. The calibration of the instruments was verified before, during, and after the entire measurement campaign. The minimum I-131 activity in the thyroid that could be detected by this device is in the range of 1–2 kBq (dependent on the age of the subject). Detailed description of the measurements is presented in Refs. [3–5].

The measurements of iodine-131 content in the thyroid gland of 1441 inhabitants of the contaminated Bryansk region were performed by specialists of the Bryansk regional Oncological Hospital during May and June 1986. The results of the measurements, which are available in our database, are related to the following five districts and for Bryansk city [4]: Gordeevskiy (510 kBq/m^2 of Cs-137 ground deposition density), Krasnogorskiy (535 kBq/m^2), Novozybkovskiy (736 kBq/m^2), Klintsovskiy (343 kBq/m^2), and Klimovskiy (200 kBq/m^2). The measurements were done by "GAMMA" equipment (Hungary) with scintillation NaI(Tl) probe supplied by lead collimator. All measurements were performed in integral mode with discrimination of the low gamma energy component. Therefore, two measurements had been done: first, over the thyroid gland, and second, over the hip area. The second measurement was selected in order to evaluate the caesium-137 input readings from the thyroid. The calibration of the equipment was done everyday using adult neck phantom and 20-ml solution with standard iodine-131 activity. Detailed description of the measurements is presented in Refs. [4,5].

The results of the direct measurements of I-131 thyroid content were used as the basis for individual thyroid dose estimations. The obtained thyroid measurements gave information related to the thyroid dose rate at the time of the measurement. In order to estimate the individual thyroid dose, it is necessary to have information on the dynamics of I-131 intake before and after the measurement. Only relative information is needed because the thyroid measurement provides a point of reference upon which the activity in the thyroid can be "tuned". For such kind of individual dose calculation, the model of dynamics of I-131 intake was used. This model provided dose calculations, taking into account the age, the moment of beginning and ceasing of the person's stay in the contaminated territories, food consumption peculiarities (milk and leafy vegetables, including the date of the consumption stop), respiratory uptake, dynamics of prolonged I-131 fallout, and dates of the beginning of the local pasture period. The description of this model is presented in Refs. [3–5]. The dates of the beginning of the local pasture period were provided in 1996 by the specialists of the Institute of Agriculture Radiology [4,5]. The dynamics of the prolonged I-131 fallout was adopted according to the recently published data [6]: as in Obninsk town (Kaluga region) for Kaluga's districts and as in Gomel city for the southwestern districts in the Bryansk region.

For the individual thyroid dose estimation, the results of questioning during the course of the measurements were used as well. The interviews included the questions concerning: age at the moment of accident, address, locations from the moment of accident till the moment of the measurement, consumption and origin of the milk and leafy vegetables including stopping of this consumption, stable iodine prophylaxis.

3. Results

The individual thyroid doses were estimated for 26 724 persons from seven districts of the Kaluga region (Kaluga's database) and for 891 persons from five districts of the Bryansk region (Bryansk's database). Dose estimations were performed only for persons

Table 1
Estimated parameters of individual thyroid dose distribution in the Khvastovichskiy district of the Kaluga region (102 kBq/m^2 of Cs-137 ground deposition density)

Items[a]	Groups by age at the time of the accident[b]					
	Below 1	1–2	2–7	7–12	12–17	17 above
N	150	159	906	996	1006	3183
MID (mGy)	300	340	310	230	120	250
DA (mGy)	56	42	28	18	15	16
SD (mGy)	59	44	29	18	14	17
DM (mGy)	36	28	19	13	11	10
GSD	2.5	2.5	2.3	2.3	2.3	2.6

[a] *N* = number of records; MID = maximum individual dose; DA = arithmetic mean dose; SD = standard deviation; DM = median dose; GSD = geometric standard deviation.
[b] Including the left end while excluding the right end.

Table 2
Estimated parameters of individual thyroid dose distribution in the Zhizdrinskiy district of the Kaluga region (129 kBq/m^2 of Cs-137 ground deposition density)

Items[a]	Groups by age at the time of the accident[b]					
	Below 1	1–2	2–7	7–12	12–17	17 above
N	153	117	646	549	620	609
MID (mGy)	550	350	430	200	180	110
DA (mGy)	110	78	48	29	24	15
SD (mGy)	81	62	43	25	24	15
DM (mGy)	85	57	34	20	15	9.6
GSD	2.0	2.2	2.2	2.4	2.6	2.6

[a] *N* = number of records; MID = maximum individual dose; DA = arithmetic mean dose; SD = standard deviation; DM = median dose; GSD = geometric standard deviation.
[b] Include the left end while exclude the right end.

Table 3
Estimated parameters of individual thyroid dose distribution in the Ulianovskiy district of the Kaluga region (191 kBq/m^2 of Cs-137 ground deposition density)

Items[a]	Groups by age at the time of the accident[b]					
	Below 1	1–2	2–7	7–12	12–17	17 above
N	144	157	780	802	705	265
MID (mGy)	520	530	460	320	250	140
DA (mGy)	80	88	56	29	26	21
SD (mGy)	66	83	50	28	27	21
DM (mGy)	60	62	42	22	18	15
GSD	2.1	2.3	2.2	2.2	2.4	2.3

[a] *N* = number of records; MID = maximum individual dose; DA = arithmetic mean dose; SD = standard deviation; DM = median dose; GSD = geometric standard deviation.
[b] Including the left end while excluding the right end.

Table 4
Estimated parameters of individual thyroid dose distribution in the Lyudinovskiy district of the Kaluga region (102 kBq/m^2 of Cs-137 ground deposition density)

Items[a]	Groups by age at the time of the accident[b]					
	Below 1	1–2	2–7	7–12	12–17	17 above
N	283	233	2631	1331	587	559
MID (mGy)	200	100	130	100	120	54
DA (mGy)	38	25	14	12	9.3	8.7
SD (mGy)	31	18	11	8.4	8.1	6.6
DM (mGy)	30	20	12	11	7.5	7.0
GSD	2.0	1.9	1.8	1.7	1.9	1.9

[a] *N* = number of records; MID = maximum individual dose; DA = arithmetic mean dose; SD = standard deviation; DM = median dose; GSD = geometric standard deviation.
[b] Including the left end while excluding the right end.

Table 5
Estimated parameters of individual thyroid dose distribution in the Kuibishevskiy district of the Kaluga region (39 kBq/m^2 of Cs-137 ground deposition density)

Items[a]	Groups by age at the time of the accident[b]					
	Below 1	1–2	2–7	7–12	12–17	17 above
N	104	65	658	694	558	179
MID (mGy)	140	78	76	50	48	36
DA (mGy)	23	24	15	11	8.8	7.2
SD (mGy)	23	17	11	7.1	6.6	5.9
DM (mGy)	13	20	12	9.1	7.2	5.4
GSD	3.0	1.8	1.9	1.8	1.9	2.1

[a] *N* = number of records; MID = maximum individual dose; DA = arithmetic mean dose; SD = standard deviation; DM = median dose; GSD = geometric standard deviation.
[b] Including the left end while excluding the right end.

Table 6
Estimated parameters of individual thyroid dose distribution in the Duminicheskiy district of the Kaluga region (75 kBq/m^2 of Cs-137 ground deposition density)

Items[a]	Groups by age at the time of the accident[b]					
	Below 1	1–2	2–7	7–12	12–17	17 above
N	173	154	926	1097	720	451
MID (mGy)	170	130	170	110	54	85
DA (mGy)	31	25	17	12	9.8	8.9
SD (mGy)	28	18	15	11	8.3	9.0
DM (mGy)	23	20	14	9.4	7.5	6.3
GSD	2.2	2.0	2.0	2.0	2.1	2.3

[a] *N* = number of records; MID = maximum individual dose; DA = arithmetic mean dose; SD = standard deviation; DM = median dose; GSD = geometric standard deviation.
[b] Including the left end while excluding the right end.

Table 7
Estimated parameters of individual thyroid dose distribution in the Kozelskiy district of the Kaluga region (41 kBq/m^2 of Cs-137 ground deposition density)

Items[a]	Groups by age at the time of the accident[b]					
	Below 1	1–2	2–7	7–12	12–17	17 above
N	68	104	944	971	801	486
MID (mGy)	80	82	89	56	45	27
DA (mGy)	12	12	6.4	4.3	3.0	2.4
SD (mGy)	14	11	6.5	4.0	3.3	2.6
DM (mGy)	6.3	8.1	4.6	3.6	2.5	1.9
GSD	3.0	2.4	2.3	1.8	1.9	2.0

[a] *N* = number of records; MID = maximum individual dose; DA = arithmetic mean dose; SD = standard deviation; DM = median dose; GSD = geometric standard deviation.
[b] Including the left end while excluding the right end.

Table 8
Estimated parameters of individual thyroid dose distribution in all the seven investigated districts of the Kaluga region

Items[a]	Groups by age at the time of the accident[b]					
	Below 1	1–2	2–7	7–12	12–17	17 above
N	1075	989	7491	6440	4997	5732
MID (mGy)	550	530	460	320	250	250
DA (mGy)	52	43	23	15	14	13
SD (mGy)	58	52	29	17	17	15
DM (mGy)	31	26	14	10	8.3	8.1
GSD	2.7	2.7	2.6	2.4	2.7	2.7

[a] *N* = number of records; MID = maximum individual dose; DA = arithmetic mean dose; SD = standard deviation; DM = median dose; GSD = geometric standard deviation.
[b] Including the left end while excluding the right end.

Table 9
Estimated parameters of individual thyroid dose distribution in the five investigated districts of the Bryansk region

District	Arithmetic mean dose (mGy)	Median dose (mGy)[a]	Number of adults
Gordeevskiy	120	74	75
Klimovskiy	48	31	9
Klintsovskiy	62	41	10
Krasnogorskiy	223	143	93
Novozybkovskiy	46	30	83

[a] Geometric standard deviation is 2.7.

with available personal information (at least age, address, and location). It should be noted that there were no countermeasures for the Kaluga region and for the Klimovskiy district of the Bryansk region [4]. For the Gordeevskiy, Klintsovskiy, and Krasnogorskiy districts, the date of introducing countermeasures is 10 May 1986 (the date for Novozybkovskiy district is 05 May 1986) [4].

It was found that individual thyroid dose distributions are very similar to the log normal type of statistical distribution [3–5]. Tables 1–8 provide the main experimental parameters of such kind of distributions for seven districts in Kaluga's database, where a lot of measurements were performed: number of records, maximum individual dose (MID), mean arithmetical dose (DA) and standard deviation (SD), median dose (DM) and geometric standard deviation (GSD) for different age groups. Table 9 presents the mean and median thyroid doses for adult persons in five districts of the Bryansk region. All doses are presented in mGy.

The obtained data were used for the validation of the semi-empirical model for thyroid dose reconstruction [4]. This allowed the reconstruction of the mean doses for Russian settlements in the contaminated territories of the Bryansk, Kaluga, Tula, and Orel regions, where I-131 measurements were not performed [5]. The dynamics of I-131 fallout and the dates of the beginning of the local pasture period were taken into account. The values of the collective thyroid doses for the Bryansk and Kaluga regions were estimated as 72 600 and 3400 persons-Gy (for population of 1 137 100 and 213 500 inhabitants). The corresponding values for the Tula and Orel regions are 13 400 and 16 900 persons-Gy (for population of 1 310 100 and 448 000 inhabitants).

4. Discussion

Re-evaluation of the thyroid doses for the Russian contaminated territories were based on the available data, including dynamics of I-131 fallout and of the beginning of the pasture period. Efforts are now underway to refine the performed dose estimates in a second run and to assess the appropriate dose uncertainties. The following activities are in progress now: development of a method of thyroid dose reconstruction based on measurements of the deposition density of I-129 (for the territories where I-131 measurements were not performed—see paper by Hoshi et al. in this issue); more correct dose estimation, including the wet or dry types of fallout (for the territories where this information is not available—see Ref. [7] concerning "birch tree effect" as an indicator of fallout type).

5. Conclusions

Re-estimations of individual thyroid doses for Kaluga's and Bryansk's databases (27 615 total personal values) were based on recently published data concerning dynamics of fallout and the dates of the pasture period. According to new estimations, the median of individual dose values in the Kaluga database (seven raions) varies from 30 mGy for children to 8 mGy for adults (GSD about 2.6). In the database of Bryansk (five raions), the median dose values are ranging from 140 mGy for children to 30 mGy for adults (GSD about 2.7). The obtained data were used for the validation of the semi-empirical model for thyroid dose reconstruction. This allowed the reconstruction of the mean doses for the settlements, where I-131 measurements were not performed. The new estimations of collective doses differ from those which were published before [2,8]. The collective thyroid doses for the Bryansk and Kaluga regions were estimated as 72 600 and 3400 person-Gy (for population of 1 137 100 and 213 500 inhabitants). The corresponding values for the Tula and Orel regions are 13 400 and 16 900 person-Gy (for population of 1 310 100 and 448 000 inhabitants).

Acknowledgements

This work was supported by The Ministry of Public Health of the Russian Federation. The part of this work was supported by Hiroshima University, Japan.

References

[1] A.F. Tsyb, E.M. Parshkov, V.V. Shakhtarin, V.F. Stepanenko, V.G. Skvortsov, I.V. Chebotareva, Thyroid cancer in children and adolescents of Bryansk and Kaluga regions, in: A. Karaoglou, G. Desmet, G.N. Kelly, H.G. Menzel (Eds.), The Radiological Consequences of the Chernobyl Accident, Proceedings of the First International Conference (Minsk, Belarus, 18–22 March 1996), European Commission and the Belarus, Russian and Ukrainian Ministries on Chernobyl Affairs, Emergency Situation and Health, Luxembourg, 1996, pp. 691–698, EUR 16544 EN.

[2] L.A. Ilyin, M.I. Balonov, L.A. Buldakov, V.N. Buriak, K.I. Gordeev, S.I. Dementev, I.G. Zhsakov, G.A. Zubovsky, A.I. Kondrusev, Yu. Konstantinov, I.I. Linge, I.A. Likhtarev, A.M. Liaginskaya, V.A. Matyukhin, O.A. Pavlovsky, A.I. Potapov, A.E. Prisiazsnyuk, P.V. Ramsaev, A.E. Romanenko, M.N. Savkin, N.T. Starkova, N.D. Tronko, A.F. Tsyb, V.F. Stepanenko, V.K. Ivanov, Ecological peculiarities, medical and biological consequences of the Chernobyl accident, Med. Radiol. 34 (11) (1989) 59–81 (in Russian).

[3] A.F. Tsyb, E.G. Matveenko, V.F. Stepanenko, V.A. Pitkevich, et al., Results of dosimetrical and medical investigation of the population in the Kaluga region after the Chernobyl accident. Report to the Ministry of Public Health. Part 1 and Part 2. Obninsk: MRRC RAMS, 1986 (in Russian).

[4] V.T. Khrousch, Yu.I. Gavrilin, S.M. Shinkarev, A.B. Smirnov, A.B. Rusanova, O.E. Ivanova, V.F. Stepanenko, A.E. Kondrashov, E.K. Yaskova, D.V. Petin, K.P. Makhonko, M.Yu. Orlov, E.V. Spirin, N.N. Isamov, M.I. Balonov, I.A. Zvonova, A.A. Bratilova. Systematisation of thyroid doses in residents of Russian territories contaminated as a result of the Chernobyl accident. Report 6.5.1.6.2-96 to the Ministry of Public Health of Russia (with Supplements). Moscow: IBPh, 1996 (in Russian).

[5] V.F. Stepanenko, A.F. Tsyb, E.M. Parshkov, V.V. Shakhtarin, A.E. Kondrashov, V.G. Skvortsov, E.K. Iaskova, A.I. Ivannikov, N.V. Belorukova, L.I. Moskovko, et al., Retrospective thyroid absorbed doses estimation in Russia following the Chernobyl accident: progress and application to dosimetrical evaluation of childhood thyroid cancer morbidity, in: M. Hoshi, J. Takada, R. Kim, Y. Nitta (Eds.), Effects of Low-level Radiation for Residents Near Semipalatinsk Nuclear Test Site, Proceedings of the Second Hiroshima International Symposium, Hiroshima University, Hiroshima, 1996, pp. 31–84.

[6] K.P. Makhonko, E.G. Kozlova, A.A. Volokitin, Radioiodine accumulation on soil and reconstruction of doses from iodine exposure on the territory contaminated after the Chernobyl accident, Radiation and Risk, Bulletin of the National Radiation and Epidemiological Registry, English Translation of Russian issue N7, 1997, pp. 90–142, Cambridge, MA.

[7] V.F. Stepanenko, Yu.I. Gavrilin, V.P. Snykov, V.E. Shevchuk, H.Y. Göksu, P.G. Voillequé, M.Yu. Orlov, Elevated exposure rates under inclined birch trees indicate the occurrence of rainfall during radioactive fallout from Chernobyl, Health Phys. 2001 (in press).

[8] I.A. Zvonova, M.I. Balonov, Radioiodine dosimetry and prediction of consequences of thyroid exposure of Russian population following the Chernobyl accident, The Chernobyl Papers, 1993, pp. 71–126, Richland, WA.

Postscript

The achievements of the first stage of the Chernobyl Sasakawa Health and Medical Cooperation Project have already been published as a book (*Chernobyl: A Decade*, Elsevier, Amsterdam, ICS1156, 1997). That volume includes detailed data collected in the 5-year examinations at the five centers. To continue the medical support for radiation-exposed victims, especially for children, several new projects were launched, mainly in the Gomel region of Belarus, beginning in 1996 and reaching completion at the end of April 2001.

Despite the difficulties of the socio-economic state of the former USSR, each center has made enormous efforts in the last five years to continue medical screening around Chernobyl according to its own budget. These activities contributed enormously to the improvement of health and welfare in each locality, especially for children. The five centers reported their activities and follow-up data carefully during the second stage of the Chernobyl Sasakawa Project. Unfortunately, we could not evaluate their data by direct comparison to the same level as we had been able to do in the first stage, because the data were not always based on a common protocol or standardized procedures. However, the principal approaches to medical diagnosis were exactly the same as those introduced and guided by us in the first stage of the project. The staff of the five centers handled and analyzed their own data and presented the results fairly concretely on the first day of the symposium.

Surveys conducted for the epidemiological studies on childhood thyroid cancer in the new Chernobyl Sasakawa Project under international cooperation have been completed. The collected data are now under statistical analysis and publication of the results in scientific journals is expected.

The present volume is unique in including scientific data in the form of invited papers as well as the overview articles from Belarus, Russia and Ukraine, which are mainly focused on wide-ranging topics of childhood thyroid cancer. The invited articles are compiled as follows the first eight papers are from non-CIS countries and the following 11 from three CIS countries.

The editors would like to thank all authors of invited papers for their contribution to enriching this volume. Although we had to confine the papers to those on the main topics of the symposium and those on radiation-related childhood thyroid cancer, many leading scientists reported medical, epidemiological and dosimetry data on the Chernobyl accident. Each invited manuscript has been minimally edited in the same format.

Finally, we would like to extend our deep gratitude to the many people involved in this project over the last ten years, and especially to the staff of the Moscow and Tokyo offices of Sasakawa Memorial Health Foundation for their continuous support.

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International Congress Series 1234 (2002) 331–349

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