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<th>Title</th>
<th>Long-term follow-up of thyroid cancer in children in Ukraine: dosimetry, epidemiology, pathology, molecular biology, pp. 1-17; 2014</th>
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<td>Author(s)</td>
<td>Saenko, Vladimir; Bogdanova, Tetiana; Tronko, Mykola; Yamashita, Shunichi</td>
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<td>© 2014 M. Tronko, T. Bogdanova, V. Saenko, I. Likhtarov, G. A. Thomas, S. Yamashita; © 2014 Nagasaki Association for Hibakushas’ Medical Care (NASHIM)</td>
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Overview of the Chernobyl accident and its consequences

The accident at Chernobyl nuclear power station was the worst technogenic catastrophe of the last century that involved radiation. Massive releases of radioactive substances led to radioactive contamination of territories surrounding the accident site through fallouts. Before Chernobyl, the only experience of massive radiation exposure known to humankind was the A-bombings of Hiroshima and Nagasaki in 1945. The character of radiation exposure of population after Chernobyl was principally different from that in Japan: protracted versus acute single dose, mostly internal versus external irradiation, influence of the different spectra of isotopes, irregular and patchy radioactive contamination of the environment, radiation exposure of millions of all ages. That is why many consequences related to health, radioecology and society could not be anticipated or reliably estimated quickly.

In this chapter we overview some technical aspects of the accident and information on radioactive releases that caused contamination of territories in the former Soviet Union countries – Ukraine, Belarus and Russia. We also describe the major groups of population affected by the accident and consider their dosimetric information. Epidemiological and medical studies from the early stages of the accident until present and their most salient results will be described. Finally, the comparative epidemiological information on thyroid cancer, one of the major health consequences of the accident, particularly focusing on the resident of contaminated territories will be given to compare the three affected countries. Note that the detailed epidemiological analysis of thyroid cancer in Ukraine after Chernobyl is presented in Chapter 3 of this book.

The accident at Reactor Number 4 of the Chernobyl Nuclear Power Plant (CNPP) located at the north of Ukraine close to the junction of the borders of the three states, Ukraine, Belarus and Russia, took place shortly after midnight on April 26, 1986. According to UNSCEAR [1], the course of events could be briefly summarized as follows. Due to some reactor design drawbacks and human errors during experimental operations immediately preceding the accident, irregular fuel overheating and fragmentation in the active zone led to the rapid transfer of excessive heat to the coolant water and induced the shock wave breaking the primary coolant system pipeline joints. Leaked water instantaneously turned to steam; this first explosion caused the reactor core displacement during which the remaining cooling water flew out of the system. Without coolant, part of the fuel vaporized because of overheating, eventually resulting in a large explosion that destroyed the reactor and
the building, and dispersed reactor debris and radioactive materials to CNPP, plant vicinity and into the environment. The initial fires that occurred after the major explosion were put under control by the end of the night of the accident. However, fuel materials remaining at meltdown site grew hot, ignited combustible products formed in the disrupted core milieu and caused an explosion-like fire. Tremendous efforts have been made to extinguish this fire, including dumping of various fission- and fire-control materials from helicopters, but the radioactive releases continued for approximately 10 more days [2,3].

There were 7 deaths during the first night of the accident: two staff members and five firemen in fire fighting actions. Among 237 firemen and CNPP employees examined within several next days for acute radiation sickness, manifestations of such of varying degrees of severity were found in 134 individuals. Despite the intensive therapy, including 13 bone marrow transplantations, 28 patients died within 4 months after the accident for various causes of death among which myelosuppression was the major reason. Nineteen more deaths were registered until 2004; in these cases bone marrow failure was unlikely the underlying cause [4].

According to the estimates, the release of radioactivity from the destroyed reactor totaled to about 13 EBq (1 EBq = 10^{18} Bq) [1,5,6]. The main radionuclides are listed in Table 1.1 of which \(^{131}\)I and \(^{137}\)Cs are radiologically most significant.

Radioactive emissions from CNPP were characterized by a wide spectrum of physicochemical forms and composition: gaseous, steam aerosol, aerosol mixtures, fuel particles, mineral particles with entrapped radionuclides, aggregates of different mineral particles, and organic compounds. The composition varied from monoelement noble gases and atomic iodine or ruthenium, to multi-element compounds and aggregates, fuel components, graphite, silicates and others, each with different radionuclide proportions [5].

Over 90% of \(^{90}\)Sr, \(^{141,144}\)Ce, and isotopes of Pu and \(^{241}\)Am were released in the form of fuel particles measuring 10 μM and less [5]. 75% of \(^{137}\)Cs contamination within the exclusion zone (the 30-km zone around CNPP) could be attributed to this physical form. At longer distances, contamination of the territories in European countries was due to steam-aerosol and gaseous mixtures, and to the particles of submicron size, containing \(^{103,106}\)Ru, \(^{131,133}\)I, \(^{132}\)Te, \(^{134,137}\)Cs and radioactive noble gases. The same isotopes were also detected in Pacific and Atlantic Oceans, and even in fallouts in Americas and Asia thus displaying the global scale of the accident. After a protective sarcophagus (object «Shelter») was upbuilt around the destroyed reactor and the building in November 1986, active emissions into the environment were not practically observed [1,2].

The dynamic meteorological conditions, including the wind, cloudiness, temperature, humidity, precipitations and their intensity in combination with varying physicochemical characteristics of radioactive materials released at different times after the reactor destruction defined the inhomogeneous pattern of the ground contamination [7,8,9]. Figure 1.1 demonstrates reconstructed plume traces over the part of Europe.

Further monitoring of the territories allowed establishing contamination pattern based on average \(^{137}\)Cs deposition densities (this isotope is easy to measure, has a long half-life and is radiologically significant) as shown in Figure 1.2 for the territories around Chernobyl. The highest density of contamination is observed in CNPP vicinity; however the levels exceeding expected background could be detected as far as up to 3000 km from the accident site.
### Table 1.1
Principal radionuclides released due to the Chernobyl accident*

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Half life</th>
<th>Activity released, PBq</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Noble gases</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{85}$Kr</td>
<td>10.72 y</td>
<td>33</td>
</tr>
<tr>
<td>$^{133}$Xe</td>
<td>5.25 d</td>
<td>~6,500</td>
</tr>
<tr>
<td><strong>Volatile elements</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{129m}$Te</td>
<td>33.6 d</td>
<td>240</td>
</tr>
<tr>
<td>$^{132}$Te</td>
<td>3.26 d</td>
<td>~1,150</td>
</tr>
<tr>
<td>$^{131}$I</td>
<td>8.04 d</td>
<td>~1,760</td>
</tr>
<tr>
<td>$^{133}$I</td>
<td>20.8 h</td>
<td>~2,500</td>
</tr>
<tr>
<td>$^{134}$Cs</td>
<td>2.06 y</td>
<td>~47</td>
</tr>
<tr>
<td>$^{137}$Cs</td>
<td>13.1 d</td>
<td>36</td>
</tr>
<tr>
<td>$^{137}$Cs</td>
<td>30.0 y</td>
<td>~85</td>
</tr>
<tr>
<td><strong>Elements with intermediate volatility</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{89}$Sr</td>
<td>50.5 d</td>
<td>~115</td>
</tr>
<tr>
<td>$^{90}$Sr</td>
<td>29.12 y</td>
<td>~10</td>
</tr>
<tr>
<td>$^{103}$Ru</td>
<td>39.3 d</td>
<td>&gt;168</td>
</tr>
<tr>
<td>$^{106}$Ru</td>
<td>368 d</td>
<td>&gt;73</td>
</tr>
<tr>
<td>$^{140}$Ba</td>
<td>12.7 d</td>
<td>240</td>
</tr>
<tr>
<td><strong>Refractory elements (including fuel particles)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{95}$Zr</td>
<td>64.0 d</td>
<td>84</td>
</tr>
<tr>
<td>$^{99}$Mo</td>
<td>2.75 d</td>
<td>&gt; 72</td>
</tr>
<tr>
<td>$^{141}$Ce</td>
<td>32.5 d</td>
<td>84</td>
</tr>
<tr>
<td>$^{144}$Ce</td>
<td>284 d</td>
<td>~ 50</td>
</tr>
<tr>
<td>$^{239}$Np</td>
<td>2.35 d</td>
<td>400</td>
</tr>
<tr>
<td>$^{238}$Pu</td>
<td>87.74 y</td>
<td>0.015</td>
</tr>
<tr>
<td>$^{239}$Pu</td>
<td>24,065 y</td>
<td>0.013</td>
</tr>
<tr>
<td>$^{240}$Pu</td>
<td>6,537 y</td>
<td>0.018</td>
</tr>
<tr>
<td>$^{241}$Pu</td>
<td>14.4 y</td>
<td>~2.6</td>
</tr>
<tr>
<td>$^{242}$Pu</td>
<td>376,000 y</td>
<td>0.00004</td>
</tr>
<tr>
<td>$^{242}$Cm</td>
<td>18.1 y</td>
<td>~0.4</td>
</tr>
</tbody>
</table>

* Decay corrected to 26 April 1986
Data are inferred from refs. [2,8,17,20]

Territories of Belarus, Ukraine and Russia were affected by the accident most heavily, as specified in Table 1.2. From the total $^{137}$Cs activity of about 64 TBq (1.7 MCi) deposited in Europe in 1986, Belarus received 23%, Russia - 30% and Ukraine - 18% resulting in radioactive contamination of approximately 3% of the European part of the former Soviet Union [10]. There were also contaminated areas in Austria, Finland, Germany, Norway, Romania and Sweden.
Table 1.2
European countries contaminated by Chernobyl fallout in 1986*

<table>
<thead>
<tr>
<th>Area with $^{137}$Cs deposition density range (per km²)</th>
<th>37-185 kBq/m²</th>
<th>185-555 kBq/m²</th>
<th>555-1480 kBq/m²</th>
<th>&gt;1480 kBq/m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Russian Federation</td>
<td>49800</td>
<td>5700</td>
<td>2100</td>
<td>300</td>
</tr>
<tr>
<td>Belarus</td>
<td>29900</td>
<td>10200</td>
<td>4200</td>
<td>2200</td>
</tr>
<tr>
<td>Ukraine</td>
<td>37200</td>
<td>3200</td>
<td>900</td>
<td>600</td>
</tr>
<tr>
<td>Sweden</td>
<td>12000</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Finland</td>
<td>11500</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Austria</td>
<td>8600</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Norway</td>
<td>5200</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>4800</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Switzerland</td>
<td>1300</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Greece</td>
<td>1200</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Slovenia</td>
<td>300</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Italy</td>
<td>300</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Republic of Moldova</td>
<td>60</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* Based on refs. [1,9]

An important role in radioactive contamination of the environment was played by radioactive $^{131,132,133,135}$I isotopes, which are short-lived radionuclides belonging to the group of light volatile substances. It is worth mentioning, however, that only $^{131}$I has a high radiological significance. Among other isotopes, only $^{133,135}$I could increase the general exposure dose, especially for the thyroid, but due to their short half-lives their effect is restricted to the areas within the near zone around CNPP.

Because of the rapid decay of $^{131}$I, collection of a large number of samples for detailed analysis was difficult [11]. However, the results of model calculations based on the limited number of measurements and determinations of $^{131}$/different radionuclide ratios, especially $^{137}$Cs (which varied 5-60-fold in different measurements), allowed reconstruction of contamination density maps [1,5,12]. The most contaminated in Ukraine, are 6 northern and central regions: Cherkasy, Chernihiv, Kyiv, Rivne and Zhytomyr regions, and Kiev-city (Fig. 1.3). In Belarus, the 3 regions in the east and south-east: Brest, Gomel and Mogilev; and in Russia 4 south-western regions: Bryansk, Kaluga, Tula and Orel. The refined $^{131}$I contamination data were considered by UNSCEAR and enabled calculation of thyroid dose estimates [13]. This is essential for radiation epidemiology and public health assessment of health consequences of the accident.

Most radionuclides released by the accident have already decayed. Attention over the next few decades will likely to be paid to $^{137}$Cs and $^{90}$Sr; the latter remains more important in the areas close to CNPP [5].
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Figure 1.1. Calculated plume formation according to meteorological conditions for radioactive releases on corresponding dates just after the Chernobyl accident [7].

Figure 1.2. Ground deposition of $^{137}$Cs in Ukraine, Belarus, and Russia around the accident site [1].
There are three major categories of individuals considered for estimation of radiation health effects after Chernobyl. These are the workers involved in the actions during the accident or in the aftermath mitigation, evacuated persons and residents of contaminated territories. They all were exposed to radiation at different time after the accident, under different circumstances and to different spectra and amounts of radioactive elements. Thus, accumulated effective doses are quite different between the groups and furthermore there are large uncertainties in dose estimates.

The first category is further subdivided into those who were at CNPP during the first day of the accident and took part in emergency measures, and those who were engaged into recovery operations from 1986 to 1990. In the literature these workers are often and collectively referred to as “liquidators”, the term officially introduced in the former Soviet Union. There were about 600 emergency workers at CNPP during May 26, and about 600,000 of liquidators including both civilians and servicemen until 1990. Estimated external doses in 134 emergency workers with acute radiation sickness manifestations ranged 0.8-16 Gy being noticeably higher than internal doses calculated to be between 0.021 and 4.1 Gy for the thyroid in 23 firemen who died of bone marrow failure [14]; it was suggested that the lower thyroid doses might have been due to stable iodine pills taken by emergency workers. Among liquidators, the average effective doses ranged from 15 mSv to 170 mSv with individual variations from <10 mSv to >500 mSv in 1986-87 [1]. Internal exposures to
the thyroid might have ranged from <0.15 Gy to 3 Gy with an average of 0.21 Gy in those who took part in the activities in and around CNPP during the first few months after the accident [15] as short-lived radioiodine isotopes largely decayed after that.

There has been also the massive evacuation of residents of the nearest settlements depending on radiological situation and the distance from CNPP [16-19]. On April 27, about 50,000 persons were evacuated from the town of Pripyat located 3 km from CNPP, where most employees and their families resided before the accident. During 10 days after the accident, through May 7, 1986, a similar number of persons who lived inside the 30-km zone surrounding CNPP were evacuated in Ukraine and Belarus. Active evacuations continued until September, 1986 and totaled in about of 116,000 relocation, mostly from Ukraine and Belarus. Estimates of external effective doses reconstructed for about 30,000 residents of the 30-km zone indicate the range from 0.1 mSv to 380 mSv with an average of 17 mSv [20]. Mean thyroid doses from $^{131}$I, based on about 5,000 direct measurements and about 10,000 questionnaires collected from Ukrainian evacuees were 0.11-3.9 Gy in children, 0.066-0.39 Gy in adolescents and 0.066-0.40 Gy in adults [21,22]. In Belarussian evacuees the estimates are 1-4.3 Gy, 1 Gy and 0.68 Gy, respectively [23]. Concordantly, these investigations have demonstrated an inverse correlation between thyroid dose and age at exposure.

With regard to the residents of contaminated territories, reconstructed maps of soil contamination with $^{137}$Cs (Figure 1.2) taken together with demographic data for Belarus, Russia and Ukraine indicate that population of contaminated territories (i.e. with $^{137}$Cs levels exceeding 37 kBq/m$^2$) was above 5 million at the time of accident, with about 1 million of children (<15 years old) and approximately 200,000 adolescents. Since the number of residents of contaminated territories is substantially greater than in the two categories of exposed persons described above, and also because the residents include individuals of all ages who might have been exposed to diverse radiological conditions at different geographical locations, dose estimates in them are more complicated and are intrinsically associated with uncertainties particularly seen in the differences between averaged collective and individual doses. Models of accumulated dose from external sources are based on soil $^{137}$Cs contamination levels and are normalized to isotope deposition density. Estimates of external doses range from 11 μSv/kBq/m$^2$ to 24 μSv/kBq/m$^2$ in 1986 for contaminated territories of the three countries being higher in rural and lower in urban areas [1]. Study of external doses in one contaminated settlement in Russia in 1987 found individual external doses to be within 2-13 mGy range with a mean of 5 mGy [24]. Internal doses for the thyroid rely on direct thyroid measurements (several hundred thousand have been taken cumulatively after the accident), individual questionnaires and computer modeling. Estimates indicate that the doses varied in a wide range from <0.05 mGy to >2 Gy in Belarussian, Russian and Ukrainian individuals of all age groups with averages of <0.3-0.7 Gy in children and individual doses up to 10 Gy [25-31]. Thyroid doses exceeding 2 Gy were observed almost exclusively in younger children aged less than 4 years [31] and they usually were higher in the residents of rural than in urban areas with similar contamination level [30]. More detailed information on thyroid dosimetry is presented in Chapter 2 of this book.

Organized administration of prophylactic or thyroid-blocking doses of stable iodine was not common. According to some surveys, from1% to about 25% of the residents of contaminated territories reported taking KI pills shortly after the accident but the recall rate was low [30,32]. In part this was due to poor preparedness to large-scale accidents such as
one that happened at CNPP, and in part to inappropriate information from the authorities. An official announcement in mass media appeared only two days after the reactor was destroyed on April 28. The delay was caused initially by the insufficient understanding of the accident scale as well as apprehension of possible massive panic. It might be expected that if clear instructions on essential safety measures have been delivered swiftly and timely (e.g. taking KI pills, not consuming fresh milk and vegetables grown in the open plots, not going outside, etc.), health consequences, at least for the residents of contaminated territories, would be less dramatic. Cost-benefit analysis performed in Belarus for 2,566 thyroid cancers in children and adolescents diagnosed and treated during 1990-2005 showed that if potassium iodide prophylaxis had been done, budget expenditures would have decreased for $400,000 per 100,000 of population [33].

The scale of the accident and the number of people affected by it were unprecedented; therefore initially it was very difficult to predict possible health consequences. In 2002, S. Nagataki, evaluating state of knowledge about Chernobyl, designated the major post-accident periods as follows: 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 investigations carried out to the future [34].

First health screenings in the most contaminated areas around Chernobyl were started shortly after the accident, mostly through local medical authorities. Only from 1990, after the request from the Government of the former Soviet Union in October 1989, international efforts were initiated to last until nowadays.

The first important collaboration was the International Chernobyl Project coordinated by IAEA. During 1990-91, the 200 experts from 25 countries examined health state including hematological, cardiovascular and thyroid disease, radiogenic cataract, cancer prevalence, fetal abnormalities and mental health for possible radiological consequences in a total of 825,000 people of 2,225 settlements in the three affected states [35]. One of the purposes was also to evaluate undertaken measures and to develop health-related advices for population residing in contaminated areas. The major findings of this project generally confirmed previously established surface contamination levels; the whole body lifetime doses were estimated not to exceed 160 mSv being several times lower than initial estimates of about 350 mSv; actual thyroid doses were difficult to confirm; stress and anxiety in the population were significant but apparently not radiation-related; no increase in leukemia or solid cancers was observed at that time; thyroid dose estimates in children were suggestive of the possible increase in thyroid cancer incidence in the future; extent of population evacuation and foodstuff restrictions appeared to be sometimes excessive.

In February 1990, the Government of the former Soviet Union appealed to Sasakawa Memorial Health Foundation (SMHF) of Japan to provide assistance specifically to the population of contaminated territories. SMHF in collaboration with the Japan Shipbuilding Industry Foundation (at present the Nippon Foundation) created a 5-year program at first entitled the “Chernobyl Sasakawa Health and Medical Cooperation Project”. According to the report of experts who evaluated situation in Chernobyl areas, the major concerns were fear and anxiety among the residents, poor informational support, and insufficient knowledge of health problems in the population. Therefore, the direct health examination,
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particularly in children, was identified as the highest priority task [36]. In May 1991, health checkups of children began in five health examination centers established in Kiev and Zhytomir (Ukraine), Gomel and Mogilev (Belarus), and Bryansk (Russia) with a special focus on direct thyroid dose measurement, thyroid examination and blood tests (also including hormone and antibody measurements) according to the unified protocol. To implement the project, SMHF donated to each center five mobile units equipped with whole body counters, ultrasound machines and blood analyzers, 10 buses for patients’ transportation as well as other medical and diagnostic equipment, computers, supplies and medicines. Until April 1996, 158,995 children aged 0-10 years at accident were examined. The project also supported training in Japan and on-site, expert visiting of the five centers, and educational materials and lectures for the residents. Among 120,605 analyzed patients, 585 (4.85%, range 1.01-17.69%) patients with thyroid nodules and 63 (0.52%, range 0.22-1.92%) with thyroid cancer were found with the highest rate among the residents of the most heavily contaminated Gomel region in Belarus aged 0-3 years at accident [37]. The prevalence of goiter was 18-54% but no correlation with whole body $^{137}$Cs count or the level of $^{137}$Cs contamination at the settlement of residence was observed [38]. The frequencies of hematopoietic malignancies, abnormal hematological parameters and thyroid autoimmunity also did not correlate with whole body $^{137}$Cs count or the level of $^{137}$Cs contamination [39]. The results of the project, which was the most reliable study at the time, indicated a link between thyroid cancer in children and the Chernobyl accident and pointed at the need in further investigations.

In view of a high importance of the results obtained in 1991-1996, SMHF has extended the project for 5 more years focusing on Gomel region of Belarus. A comparative study of thyroid diseases in children born before and after the accident was designed to involve 21,601 persons examined from February 1998 to December 2000 using the approaches established during the first project [40]. A total of 32 (0.15% of examined children) thyroid cancers were diagnosed of which 31 was in the group of 9,720 children born before the accident, one in a child born during April 27 - December 31, 1986 (i.e., possibly exposed in utero) while no thyroid cancers were detected in the group of 9,472 children born after the accident. The estimated odds ratios of the frequency of thyroid cancer in the group born before the accident and in utero exposed group were 121 and 11, respectively, as compared to those born after the accident. A conclusion about the likelihood of causal link between direct external or internal exposure to short-lived radionuclides including $^{131}$I and $^{133}$I was drawn.

The extended SMHF project provided a good opportunity for collaboration with the Belarus/Russia/EU/IARC epidemiological case-control study aimed at the evaluation of the risk of thyroid cancer after exposure to $^{131}$I and elucidation of risk-modifying factors. In a united effort, which initially included all individuals with thyroid cancer aged less than 15 years at the time of accident from Gomel and Mogilev regions of Belarus and from Bryansk, Kaluga, Tula and Orel regions of Russia (a total of 276 at the end of study) and at least four closely matched population-based controls (1,300 persons) were analyzed. Individual thyroid doses were reconstructed and used to estimate dose-response relationship. It was found to be significant and linear up to 1.5-2 Gy [41]. Odds ratio for thyroid cancer varied from 5.5 to 8.4 for a dose of 1 Gy according to different risk models being generally comparable with risk estimates for external exposures [42]. Importantly, a strong modifying
effect of iodine deficiency was observed: relative risk for developing cancer was 3.2 in iodine deficient areas whereas a dietary supplementation with KI reduced the risk approximately 3-fold (relative risk of 0.34). This study was the largest population-based investigation in young people living in Chernobyl areas; it provided a strong definitive evidence of causal association between the risk for thyroid cancer and internal exposure to radioiodine at young age. The major route of $^{131}$I ingestion by residents was its incorporation into food chains of pastured cattle, mostly cows, and consumption of fresh milk as well as from vegetables and fruits grown in open soil. Incorporation of $^{137}$Cs may have contributed to dose formation. That is why both $^{131}$I in the thyroid and in milk, and $^{137}$Cs in soil, food and in the body are considered for dose reconstruction [43].

The World Health Organization (WHO) has been playing an active role in studying and managing health consequences of Chernobyl. One of the largest projects was the International Project on the Health Effects of the Chernobyl Accident (IPHECA) launched in May 1991 and completed in 1996 with international budget support primarily from the Government of Japan and with the contribution from Czech Republic, Slovakia, Switzerland and Finland [44]. IPHECA included a number of pilot projects: Brain damage in utero, Epidemiological Registry, Hematology, Medical and psychological rehabilitation of Chernobyl liquidators, Oral Health, Radiation Dose Reconstruction, and Thyroid. In collaboration with SMHF project, over 210,000 children were examined. The findings were in line with the earlier SMHF projects: by the end of 1994, 565 children (208 in Ukraine, 333 in Belarus and 24 in the Russian Federation) who lived in contaminated regions were diagnosed for thyroid cancer but no significant increase in the incidence of leukemia or other blood disorders were registered [45].

In February 1999, the WHO and SMHF started the Chernobyl Telemedicine Project whose aim was to improve early diagnosis, treatment, and follow-up of patients with thyroid cancer, primarily in Gomel region of Belarus. A satellite-based telematic system was established that allowed an exchange of thyroid ultrasound and cytology images, and of related information on the patients between Thyroid Oncology Center in Minsk, the Research Center for Radiation Medicine in Gomel and Nagasaki University School of Medicine with synchronized databases [46-49]. By September 2000, information on 330 cases was entered into the database and reviewed independently thus improving diagnosis.

Another important project was the establishment of the Chernobyl Tissue Bank (CTB) in October 1998 based on funding from the European Commission, WHO, SMHF and the U.S. National Cancer Institutes and approved by the Governments of Belarus, Russian and Ukraine [50]. CTB activities and projects are described in Chapter 6 of this book.

Even at present, when major causes of health consequences of the CNPP accident, at least with regard to thyroid cancer, are clarified, international activities continue. One of them is the Chornobyl Thyroid Diseases Study Group of Belarus, Ukraine, and the USA [51]. The study follows-up a cohort of 25,161 individuals (11,918 in Belarus and 13,243 in Ukraine) born between April 26, 1968 and April 26, 1986, with direct thyroid measurements available shortly after the accident to improve individual dose estimates and to collect health-related information based on bi-annual (or annual) screenings. The project was started in December 1996 in Belarus and in April 1998 in Ukraine.
During the first screening in 1998-2000, 45 thyroid cancers were detected in Ukraine [52]. An approximately linear dose-response relationship was found with excess relative risk estimate of 5.25 per 1 Gy. The older age tended to associate with the decreased risk of thyroid cancer. A fraction of cancers attributed to radiation was estimated to be 75% (95% CI 50-93%).

Reconstruction of thyroid doses in Belarus is now ongoing for the newly evaluation of the risk of radiation-associated thyroid cancer [53]. In Ukraine, there are extensive risk analyses of thyroid cancer and of other thyroid diseases among individuals exposed in utero to $^{131}$I from Chernobyl fallout [54] as well as of that of non-cancer thyroid neoplasms [55] and autoimmune thyroiditis [56]. The results of this large-scale project are expected to further refine conclusions of the earlier, concurrent and ongoing studies.

Clean-up workers is a group exposed to radiation at the accident site. Their thyroid doses are mostly attributed to external exposures although those who took part in mitigation efforts during the first two months might have received internal doses from inhaled radioiodines.

In 1997, based on a survey of 167,862 liquidators registered in Russian National Medical Dosimetric Registry, 47 verified thyroid cancers were reported. An excess relative risk (ERR) of thyroid cancer of 5.31 per 1 Gy and an excess absolute risk of 1.15 per $10^4$ person-years/Gy were found [57]. By the end of 1998 a total of 58 thyroid cancers were diagnosed in a subset of 99,024 liquidators from 6 regions of Russia [58]. A statistically significant increase of standardized incidence rate (SIR) of thyroid cancer of 4.33 was found in this group as compared to the background rate in male population of Russia. However, dose-response relationship could not be established with ERR of -2.23 per 1 Gy (95% CI, -4.67; 0.22).

In Belarus, based on the information from National Cancer Registry, for about 120,000 liquidators in the country the standardized index of incidence for the period from 1993 to 2000 was reported to be 24.4 per 100,000 while in the adult population of the country aged more 30 years this index in 2000 was 5.67 [59].

Together these data indicate that thyroid cancer incidence is elevated in liquidators but radiation risk needs to be further clarified through continuous observations.

In exposed residents of all ages, which also include evacuated persons, an increased radiation-related risk was found in a number of epidemiological studies, as pointed above, for those who were exposed to radioiodines during very young ages. Descriptive epidemiology data on current situation with regard to thyroid cancer for the three countries is summarized below.

In Ukraine, as shown in a recent analysis of a sample set approaching in size to the whole population of the country, in 1989-2008 age-adjusted thyroid cancer incidence rate in female residents of highly exposed regions increased from 3.34 to 10.99 (3.3-fold), and from 2.51 to 5.69 (2.3-fold) in low-exposure regions per 100,000 individuals [60]. In males, age-adjusted incidence rate grew from 0.87 to 2.64 (3.0-fold) and 1.37 (1.6-fold) in highly exposed and low-exposure regions, respectively. For the patients diagnosed during childhood and adolescence, the analysis adjusted for screening and technological effects shows that incidence rate was significantly elevated in the residents of highly contaminated regions born before the accident as compared to those born after the accident while no similar difference was found for low-exposure regions. The average annual increase in
incidence was also significantly higher in the highly-exposed regions in all age subgroups in both males and females suggestive of the radiation excess of thyroid cancers not only in children and adolescents but also in adults. Interestingly, in 2006 mean incidence ratio in highly-exposed and low-exposure regions decreased in all female age subgroups and most male subgroups, which may imply that the peak of radiation excess of thyroid cancer in the country has been passed. These observations are important and need further dose-response and risk analysis for completeness.

Statistical data from the Clinico-morphological Registry at VP Komisarenko Institute of Endocrinology and Metabolism (IEM) of the National Academy of Medical Sciences of Ukraine in Kiev indicate that from 1986 to 2010 a total of 6,798 cases of thyroid cancer have been diagnosed, of which 5,044 (74.2%) in those who were children aged 0-14 years, and 1,642 (24.2%) adolescents aged from 15 to 18 years at the time of accident and also 112 (1.6%) cases of exposure in utero [ref. 61 and Chapter 3 of this book].

In Belarus, during the period from January 1985 to December 2006, 14,147 patients with primary thyroid cancer were diagnosed and treated in Thyroid Cancer Center in Minsk [62]. During over than 20 years of observations after the Chernobyl accident, the crude standardized incidence of thyroid cancer increased from 1.3 to 8.8 per 10^5 individuals. Within last five years, the number of primary thyroid cancers in patients aged 19-45 did not grow significantly. In contrast, patients above 46 years old demonstrate an increasing incidence. These tendencies are currently seen in both heavily and less contaminated regions of the country.

In Russia, according to currents data from the National Radiation Epidemiological Registry (former Russian National Medical Dosimetric Registry), a total of 9,120 thyroid cancer cases were registered for the period from 1981 to 2008 in the population of all ages from the four regions officially recognized as contaminated. In 1981-1986, 102 thyroid cancer cases were registered annually on average. By contrast, during 2002-2008 the number of detected thyroid cancer cases was growing with the maximum of 592 cases observed in 2008 thus displaying a 6-fold increase. During the pre-accident and latent periods, the crude incidence rate of thyroid cancer was 7.7 for males and 37.8 for females while for 2002-2008 it was 36.1 and 170.4, respectively, per 10^6 individuals. In a cohort of 309,130 residents of contaminated areas followed-up from 1991 to 2008 for whom individual thyroid doses were reconstructed, 993 cases of thyroid cancer were diagnosed. Of them 978 cases were histologically verified; 247 cases were in children and adolescents and 746 cases in adults [63]. Of note, the analysis in children and adolescent subgroup demonstrated a shift of the distribution functions towards the cases with the higher doses which may be indicative of radiation-related risk. Indeed, calculations indicated that a statistically significant ERR of thyroid cancer incidence is found in this subgroup with an estimate of 3.22 per 1Gy.

The tendencies in thyroid cancer incidence in different age groups of the residents of contaminated territories for Ukraine [61] and Belarus [64] are shown in Fig. 1.4. Despite the patterns between the countries may vary in details, common trends could be seen: peak incidence in childhood patients occurred in 1995-97, in adolescents in 2001-2004, and in adults a gradually increasing incidence is observed.
Overview of the Chernobyl accident and its consequences

Figure 1.4. Incidence of thyroid cancer in Ukraine, in 6 most contaminated and 21 less contaminated regions of the country, and in Belarus (for comparison) in different age groups of patients diagnosed during 1986-2006. Data for Ukraine are from ref. [61], for Belarus data are derived from ref. [64]. Lines comprise polynomial best-fit of data for easier visualization.

Regarding radiation-related risk, it is well proven that such does exist in exposed children and adolescents while the question still remains open for exposed adults. It has been proposed, with reservations, that radiation excess of thyroid cancers may be observed in the group of population exposed at older ages as well as that latency of thyroid cancer may be proportional to age in adult cancer patients subjected to radiation therapy [65]. At present, however, there is no strong evidence of radiation-related excess risk in the residents of contaminated territories exposed in adult age.

To summarize the chapter, here we overviewed the major aspects of the accident at the CNPP, and its radiological and health consequences with a particular focus on thyroid cancer. As a result of massive radioactive releases, large groups of population received radiation doses. These include clean-up workers and general population which was either evacuated from the settlements in the vicinity of CNPP shortly after the accident or continued to live in the territories of Ukraine, Belarus and Russia which were contaminated by fallouts. Health consequences were initially difficult to forecast. Besides of deterministic effects of acute exposure to ionizing radiation in firemen, information about contamination levels of the affected territories, spectrum of pollutant radionuclides and doses accumulated by
the residents were completely unknown. That is why, after first several years of domestic efforts, large scale international collaborations were initiated to address nearly any related problem, involving many governmental and non-governmental organizations from a number of countries and from the world-wide community. Through cooperative investigations, health status and dosimetric data were obtained to provide a ground for assessing the consequences. First reports about the increase of thyroid cancer incidence in children and adolescents in Belarus and in Ukraine [66,67] were met cautiously by the experts because of doubts in the accuracy of diagnosis, too short period of latency (which would expected to be about 10 years as seen from A-bombing of Hiroshima and Nagasaki) and insufficient evidence of link between Chernobyl radiation and cancer outbreak. With time, however, essential proofs were found and efforts of both health authorities in the three most affected countries and of the international parties could be focused on the high-risk groups and through more specialized means.

The accident at CNPP allowed learning a number of lessons such as that a disaster in one country may affect other, that appropriate handling of vital information about and better preparedness to radiation-involving accidents may bring about less adverse consequences, that international collaboration even on delicate issues could be established and it can be effective. In the medical area, a large experience has been accumulated, including the understanding of the possibility of very short period of latency for thyroid cancer after internal exposure to radioiodine, and how to diagnose and treat young patients with thyroid cancer.

In conclusion, while major health effects of the Chernobyl accident have become clearer after 27 years that passed, we are still far from understanding of all the consequences, even applicably to thyroid cancer. As shown recently in A-bomb survivors of Japan, the excess thyroid cancer risk associated with irradiation in childhood remained detectable over 50 years after exposure [68]. It therefore is essential to continuously and consistently observe liquidators and exposed population to achieve higher level of knowledge of radiation effects after Chernobyl.

This chapter is an updated and modified version of our review article published earlier [69].

References

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