Thyroid examination in highly radiation-exposed workers after the Chernobyl accident

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Abstract

Context: Radioactive contamination from the Chernobyl nuclear accident that happened on the morning of 26th April 1986 had a major impact on thyroid health in the Belarus region.

Objective: Observational study of a cohort of 99 adults, most strongly exposed to ionizing radioactivity.

Design, setting and patients: Observational study performed between 1998 and 2000. The cohort comprised 99 workers (92 male) of the Chernobyl nuclear power plant. Examination including physical examination, ultrasonography of the thyroid gland and measurement of serum free thyroxin (fT4), free triiodothyronine (fT3) and TSH. Anti-thyroperoxidase (anti-TPO), antithyroglobulin (anti-Tg) antibodies and thyroid stimulating immunoglobulin were also determined.

Main outcome measures: The impact of exposure to high-dose radiation, including radioactive iodine, on the thyroid gland was examined.

Results: Levels of fT4 in all probands were within the normal World Health Organization-defined range. Elevated levels of fT3 were found in two workers (2%), high titres of anti-TPO and anti-Tg antibodies were present in four subjects (4%). Mild hypothyroidism was present in one patient. Enlargement of the thyroid gland was observed in 17 workers (17%). There was no evidence of clinically overt thyroid cancer.

Conclusions: The Chernobyl accident showed surprisingly little impact on the thyroid in a cohort of workers strongly exposed to radiation. Our data suggest an age-dependent heterogeneity in response to the short-lived radioiodine isotopes and favours long-term follow-up analysis.

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Introduction

On the 26th of April 1986, reactor 4 at the Chernobyl nuclear power plant severely malfunctioned. The Chernobyl accident is the worst disaster in the history of nuclear power generation. According to recent data, the air at Chernobyl had been contaminated with about 5300 PBq radionuclide activity, including 1760 PBq (131)I and 85 PBq (137)Cs. The highest radiation was received by the liquidators (0.8–16 Gy), lower doses were received by the population that was evacuated or inhabited the contaminated areas (1–3). The released radioactivity caused a major increase in thyroid cancer in children, and led overall to an almost 100-fold increase in thyroid cancer incidence in the Belarus region (4). These thyroid cancers demonstrated an aggressive phenotype with a high prevalence of lung metastasis (5).

To evaluate the impact of the Chernobyl accident on thyroid health in a unique cohort of power-plant workers and so-called liquidators, a follow-up study (1998–2000) was conducted. These adults were most strongly exposed to the ionizing radioactivity. In this report, we describe results from a cross-sectional evaluation of 99 probands who were among the most severely irradiated employees of the Chernobyl power plant and who were originally suspected to have had acute radiation sickness (ARS).

Patients and methods

Subjects

Ninety-nine patients exposed to ionizing radiation from the Chernobyl accident and available for
follow-up at clinical centres in Kiev, Moscow and Ulm were examined between 1998 and 2000. The cohort comprised 92 male and 7 female patients with a mean age at the time of exposure of 33 years (range 21–60 years) and a mean age at follow-up examination (1998–2000) of 47 years (range 35–74 years).

Twenty-four of 99 (24%) reported regular oral iodine administration, with a maximal dose of 200 μg/day before and after the accident. Blocking of radioiodine uptake by thyroid using potassium iodide (KI) according to International Atomic Energy Agency recommendations (KI prophylaxis) had not been used in this cohort.

These patients were among the most severely exposed to high local doses of β-particle and γ radiation, either as working personnel within the reactor immediately after the accident or as members of the immediate clean-up forces (so-called liquidators) in the days following the accident. Table 1 gives histories of patients with an impairment of the thyroid gland during or immediately after the accident.

The whole-body exposure radiation dose was reported as 0.3–8.7 Gy (2). All patients were classified into four groups based on the severity of ARS in the acute phase after the accident, as previously described (6). Patient characteristics with respect to ARS severity are presented in Table 1. Twenty-two patients in the study cohort suffered from first-degree ARS, 24 from second-degree ARS, 10 from third-degree ARS, and one from fourth-degree ARS. The study cohort also included 42, so-called non-confirmed patients, who were exposed to radiation doses that were not sufficient to induce ARS. The ARS radiation doses received were, however, high enough to cause mild clinical signs and symptoms, including changes in peripheral blood counts. In 1989, a re-evaluation of the so-called non-confirmed showed that these patients did not in fact have ARS.

### Table 1 Patient characteristics according to acute radiation sickness (ARS) severity.

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<thead>
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<tbody>
<tr>
<td>Non-confirmed</td>
<td>0</td>
<td>103</td>
<td>0</td>
<td>103</td>
<td>6</td>
<td>97</td>
<td>42</td>
<td>5</td>
<td>5</td>
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<tr>
<td>I mild</td>
<td>131</td>
<td>41</td>
<td>0</td>
<td>41</td>
<td>4</td>
<td>37</td>
<td>22</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>II moderate</td>
<td>59</td>
<td>50</td>
<td>1</td>
<td>49</td>
<td>6</td>
<td>43</td>
<td>24</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>III severe</td>
<td>26</td>
<td>22</td>
<td>7</td>
<td>15</td>
<td>3</td>
<td>12</td>
<td>10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>IV very severe</td>
<td>21</td>
<td>21</td>
<td>20</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
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<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>237</td>
<td>237</td>
<td>28</td>
<td>209</td>
<td>19</td>
<td>190</td>
<td>99</td>
<td>17</td>
<td></td>
</tr>
</tbody>
</table>

ARS was confirmed in 134 cases in 1989 re-evaluations on the basis of clinical symptoms, dynamics of neutrophils, lymphocytes, and thrombocytes in peripheral blood, and chromosomal aberrations of peripheral lymphocytes.

### Physical examination

Detailed case histories were obtained and physical examinations were performed in all patients. Thyroid enlargement was determined using inspection and palpation in accordance with the WHO definition of 4 degrees: 0a, no goitre; 0b, palpable but not visible goitre; I, palpable and visible goitre at reclined head position; II, visible goitre.

### Ultrasonography

The thyroid gland was examined using a high-resolution linear ultrasonographic 7.5-MHz transducer (Aloka 630, Japan). The volume of the thyroid gland was determined as reported by Brunn and coworkers (7). Subsequently, thyroid gland enlargement, i.e. goitre, was diagnosed when the thyroid gland volume exceeded 25 ml in male or 20 ml in female patients respectively. If present, nodules were classified according to the following features: no/diffuse microcalcifications, regular/irregular margins, regular/irregular sonolucent halo and no/regional lymphadenopathy. No fine-needle biopsies have been performed and no thyroid surgery was performed after the accident.

### Lab analysis

Serum concentrations of T4, T3, and TSH were measured using highly sensitive immunometric technology (Ortho-Clinical Diagnostics GmbH, Neckargmünd, Germany). Serum levels of anti-thyroidperoxidase (anti-TPO) and antithyroglobulin (anti-Tg) antibodies were determined using a commercially available variable ELISA (Vita Diagnostica GmbH, Freiburg, Germany). The ELISA test was considered, according to the criteria of the European Thyroid Association, as detecting anti-TPO in preparations of thyroid microsomes (8). Thyroid stimulating immunoglobulin (TSI) titres were measured using a commercially available...
luminescence receptor assay (BRAHMS Diagnostica GmbH, Henningsdorf, Germany). Autoantibody titres are presented in units of IU/ml (anti-TPO, anti-Tg) or IU/l (TSI) according to a World Health Organization reference. The normal ranges for these thyroid hormones and thyroid antibodies are: fT4, 10–23 nmol/l; fT3, 1.4–2.8 nmol/l; TSH, 0.2–4.2 mIU/l; anti-Tg and anti-TPO, 0–100 IU/ml; TSI, <9 IU/l. Hypothyroidism was defined as fT4 < 10 nmol/l and TSH ≥ 3.5 mIU/l. Positive thyroid autoantibodies were defined as anti-TPO and anti-TG concentrations > 100 IU/ml and TSI concentrations > 9 IU/l.

Study probands provided written informed consent for the follow-up study.

**Results**

**Physical examination**

No clinically apparent signs of thyroid dysfunction were present in the cohort. Various degrees of thyroid gland enlargement were present in 17 of 99 patients. Nine patients had 0b-degree goitre, seven patients had degree-I goitre, and one patient had degree-II goitre (Table 2). No evidence of pressure to adjacent structures, infiltration, lymph-node enlargement or regional or distant metastasis was found on physical examination.

**Ultrasonography**

Using ultrasonography, a nodular goitre was diagnosed in 10 and a diffuse goitre in seven of the above-mentioned patients respectively (Tables 2 and 3). All nodules determined were lacking microcalcifications, irregular margins, irregular sonolucent halo and regional lymphadenopathy. Four probands revealed a solitary thyroid nodule, and six probands showed multinodularity. All nodules appeared with a regular margin and/or a well-defined sonolucent halo. No fine-needle biopsies have been performed.

**Laboratory examination**

Thyroid hormones could be determined in 74 out of 99 patients. Serum fT4 levels were within the normal range in all cases (mean ± s.d. 18 nmol/l ± 2.46, range 12.4–23.3 nmol/l). In one patient, the serum TSH level was slightly above the normal range (4.49 mIU/l), and fT4 was close to the reference minimum (11 nmol/l). This male patient had suffered from fourth-degree ARS. In 1986, he was 25 years old; at the time of examination, he was 39 years old. Two patients had elevated serum fT3 levels (2.98 and 4.15 nmol/l). There were, however, no abnormalities in fT4, basal TSH, or thyroid antibodies. Both patients were reported as having suffered second-degree ARS; their age at exposure was 25 years, and their age at examination was 40 years.

**Autoantibodies**

In four cases (three males, one female), anti-TPO antibodies were present at a markedly high concentration (mean ± s.d. 1104 IU/ml ± 1275, range 234–3000 IU/ml). Three out of these four patients also had increased anti-TG antibody titres (mean ± s.d. 1119 IU/ml ± 1629, range 202–3000 IU/ml). In three of these patients, serum fT3, fT4 and TSH concentrations

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**Table 2** Laboratory findings.

<table>
<thead>
<tr>
<th>Patient number</th>
<th>ARS severity</th>
<th>Age at examination (years)</th>
<th>Goitre</th>
<th>Thyroid hormones</th>
<th>Thyroid antibodies</th>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>TSH (MlU/l)</td>
<td>fT4 (nmol/l)</td>
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<tr>
<td>1</td>
<td>n.c.</td>
<td>63</td>
<td>0b</td>
<td>1.47</td>
<td>17.6</td>
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<tr>
<td>2</td>
<td>n.c.</td>
<td>45</td>
<td>0b</td>
<td>3.1</td>
<td>20.4</td>
</tr>
<tr>
<td>3</td>
<td>n.c.</td>
<td>48</td>
<td>I</td>
<td>1.12</td>
<td>14.4</td>
</tr>
<tr>
<td>4</td>
<td>n.c.</td>
<td>61</td>
<td>I</td>
<td>3.71</td>
<td>22.6</td>
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<tr>
<td>5</td>
<td>n.c.</td>
<td>73</td>
<td>0b</td>
<td>2.63</td>
<td>15.7</td>
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<tr>
<td>6b</td>
<td>I</td>
<td>58</td>
<td>0b</td>
<td>2.32</td>
<td>17</td>
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<tr>
<td>7</td>
<td>I</td>
<td>45</td>
<td>I</td>
<td>2.12</td>
<td>16</td>
</tr>
<tr>
<td>8</td>
<td>I</td>
<td>55</td>
<td>0b</td>
<td>1.35</td>
<td>13.3</td>
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<tr>
<td>9</td>
<td>I</td>
<td>56</td>
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<tr>
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<td>I</td>
<td>70</td>
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<td>11</td>
<td>II</td>
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<td>I</td>
<td>8.4</td>
<td>18.9</td>
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<td>II</td>
<td>64</td>
<td>I</td>
<td>3.35</td>
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<td>II</td>
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<td>II</td>
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<td>I</td>
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<tr>
<td>17</td>
<td>IV</td>
<td>40</td>
<td>0b</td>
<td>4.49</td>
<td>11</td>
</tr>
</tbody>
</table>

*a* Non-confirmed patient.

*b* Female patient.

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were within the normal range, whereas in one patient TSH was elevated to 9.4 mIU/l without corresponding changes in T1/2 and T1/3 levels. Thyroid antibodies in the antibody-positive patients were associated with clinically and sonographically observed goitre. In the antibody-positive patients, mean thyroid gland volume was 33 ml (range 28–40 ml) in males and 25 ml in the female patient. At the time of exposure, the mean age for all four patients was 47, and was 62 years at examination. Of these patients, two had suffered from second-degree ARS, one from first-degree ARS and one belonged to the non-confirmed group (Table 2 and 3).

**Discussion**

Twelve to fourteen years after the Chernobyl accident, we studied a cohort of adults who were exposed to particularly high levels of ionizing radioactivity, including a high dose of radioactive iodine (131-I, 132-I, 133-I and 135-I). This unique cohort comprised 99 long-term survivors from a group of 237 Chernobyl workers including also liquidators originally diagnosed with ARS. By contrast to what has been reported for children from the Belarus area, the impact of the Chernobyl accident on the thyroid condition in this adult cohort was found to be different. No clinically overt thyroid cancer was found.

It is well known that exposure to ionizing radiation is associated with an increase in incidence of thyroid abnormalities and in particular thyroid cancer (9–13). An increase in the incidence of thyroid cancer was observed in survivors of the atomic bomb in Japan (14) and in residents of the Marshall Islands exposed to ionize radiation during the testing of hydrogen bombs (15). Of note is the higher rate of thyroid cancer in females. The cohort addressed in our study mostly comprised men therefore reducing the likelihood of thyroid cancer per se.

In Belarus, Russia, and the Ukraine there was a marked increase in the incidence of paediatric thyroid cancer following the Chernobyl accident (16–19). Previous studies demonstrated a higher prevalence of nodular goitre in atomic bomb survivors as compared...
with individuals in control groups (20, 21). In our cohort, nodular goitre was present in only 10%. Based on the physical examination and ultrasonography, thyroid nodules observed were classified as most likely benign lesions. However, there are no ultrasound characteristics that definitively exclude carcinoma. Since fine-needle biopsies or thyroid surgery had not been performed, we can not rule out the presence of thyroid cancer.

In adults, unlike in children, other radiation-induced pathologies of the thyroid gland such as autoimmune thyroiditis may become more prevalent. In atomic bomb survivors and patients treated with external radiation for non-thyroid diseases, exposure to radiation was associated with increased incidence of thyroid autoimmunity (22–24). In our study, we also found evidence of thyroid autoimmunity. Affected patients reported pain over the thyroid gland, which suggests antibody formation due to acute radiation thyroiditis (25, 26). However, it is important to acknowledge that thyroid autoimmunity has also been described in healthy individuals with no documented exposure to ionizing radiation. In two population-based studies from the United Kingdom (Wickham Study) and Australia (Busselton Health Survey) anti-TPO prevalence rates of 6.8% and 6.6% respectively, were reported (28, 29).

In a more recent study using the same antibody detection technology as in this study, 5.1% of Caucasian healthy blood donors were anti-TPO positive (30).

A limitation of the study is that it is an observational study with no control group. In addition, the number of probands is low when compared with standard population-based evaluations. Therefore, only observational data of a very unique group of patients can be presented. Long-term follow-up including fine-needle aspiration of thyroid nodules will be needed to define the cancer risk more accurately. In view of previous observations of thyroid malignancy in radiation-exposed patients, there is still a high probability of subsequent development of thyroid malignancies. Therefore, in accordance with published data, and due to the high susceptibility of the thyroid gland to radiation damage, a detailed long-term follow-up of thyroid function during the next several decades would be of great importance in identifying thyroid malignancies and deviation of its function. Our data, however, do suggest that the pathobiology of the thyroid gland after radiation exposure is different in adults versus children (30, 31).

Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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