Precocious hypothyroidism mechanisms after radioiodine treatment in Graves’ disease

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Résumé

Mécanismes des hypothyroidies précoces survenant après traitement de la maladie de Basedow par iode radioactif

Objectif > Une hypothyroïdie peut survenir après traitement d’une maladie de Basedow par IR Athérapie. Elle est parfois précoce (moins d’un an après le traitement), voire transitoire. Le but de ce travail était de mieux comprendre les mécanismes à l’origine de ces hypothyroidies précoces en comparant les patients ayant eu une hypothyroïdie précoce et ceux n’en ayant pas développé.

Méthodes > 36 patients traités par iode radioactif ont été inclus. Les variables analysées étaient : âge, sexe, présence d’une orbitopathie basedowienne (OB), délai entre le diagnostic de la maladie et l’IR Athérapie, nombre de récidives, thérapies antérieures, corticothérapie (prescrite pour éviter l’aggravation d’une OB préexistante), masse fonctionnelle thyroïdienne, et dose d’¹³¹I administrée. Les titres de T₄ libre, thyroid-stimulating hormone (TSH), anti-TSH receptor antibodies (TRAb), anti-thyroid peroxidas (ATPO) et anti-thyroglobulin (ATG) ont été relevés. Thyroid stimulating (TSAb) et blocking (TBAb) antibodies were determined and uptake of ¹²³I was measured when hypothyroidism occurred.

Résultats > Vingt-trois patients ont développé une hypothyroïdie précoce (groupe A), alors que 13 patients ont développé une hypothyroïdie du groupe B. Les titres initiaux d’ATG étaient significativement plus élevés dans le groupe A (p = 0.0024), et corticosteroid therapy was used more frequently to avoid aggravation of an OB preexistent (p = 0.0276). TPOAb and TGAb were monitored.

Summary

Objective > Hypothyroidism can occur after radioiodine treatment for Graves’ disease. It may happen precociously and transiently in the first year after treatment. The purpose of this study was to understand the mechanisms responsible for precocious hypothyroidism.

Methods > 36 patients treated for Graves disease by radiiodine were prospectively studied; the following variables were included in the analysis: age, gender, attendance for Graves’ orbitopathy (GO), delay before radioiodine treatment, number of recurrences, previous treatments, corticosteroid therapy, thyroid mass, and ¹³¹I dose. The titres of free T4 (FT4), thyroid-stimulating hormone (TSH), anti-TSH receptor antibodies (TRAb), anti-Thyroid peroxidas antibodies (TPOAb) and anti-thyroglobulin antibodies (TGAb) were monitored. Thyroid stimulating (TSAb) and blocking (TBAb) antibodies were determined and ¹²³I uptake was measured when hypothyroidism occurred.

Results > 23 patients became precociously hypothyroid (group A) while 13 patients did not (group B). The initial TGAb titre was higher in group A (p = 0.0024), and corticosteroid therapy was used more frequently to avoid aggravating GO in group B (p = 0.0276). TPOAb and TGAb titres increased significantly only in group A (p = 0.0112 and p = 0.0202, respectively). When hypothyroidism occurred, TBAb was present in 13 patients. Transient hypothyroidism due to TBAb was observed in 1 patient. No iodide organification impairment was disclosed by the perchlorate test.
Radioiodine is one of the most efficient therapies for patients with Graves’ disease because $^{131}$I emits β-radiation that causes cell necrosis and an inflammatory response, and over time, chronic inflammation and fibrosis [1]. Surgical removal of the thyroid gland comprises another ablative therapy but carries a risk of specific complications [1]. In some centres, ablative doses of radioiodine are now deliberately used so that hypothyroidism may occur in more than 60% of the patients a few weeks or months after irradiation, warranting in some places the regular prescription of levothyroxin to prevent clinical hypothyroidism. Alternatively, in our centre like in others, radioiodine treatment purpose is to recover euthyroidism, but even in these cases, definitive hypothyroidism may happen, with a cumulated incidence of 24% at 1 year, 59% at 10 years, and 82% at 25 years [2]. The incidence is related directly to radiation damage, and hypothyroidism may occur early in the year following therapy [3]. In some patients, precocious hypothyroidism is transient, and its incidence is variable, ranging from 2.4% [4] to 58% [5].

Several mechanisms may explain precocious hypothyroidism during the first year after radioiodine treatment including precocious massive thyroid destruction [1], subacute radioinduced thyroiditis, or autoimmune disorders [6,7]. The thyroid cells destroyed by $^{131}$I treatment release thyroid antigens, such as the thyroid-stimulating hormone (TSH) receptor, which causes a transitory increase in anti-TSH receptor antibodies (TRAb) level [6,8]. Several studies have suggested that thyroid-blocking antibodies (TBAb) may be implicated in precocious hypothyroidism [9–12]. Acquired iodide organification impairment might also explain thyroid insufficiency, but to our knowledge, this hypothesis has not been tested.

The purpose of this study was to evaluate the mechanisms underlying early radioinduced hypothyroidism and to identify the involvement of functional or autoimmune disorders in its pathogenesis. We measured anti-TSH receptor antibodies (TRAb), anti-thyroid peroxidase antibodies (TPOAb) and anti-thyroglobulin antibodies (TGAb) titres in a group of patients.
with Graves’ disease who developed precocious hypothyroidism and in a group of patients who did not. In patients who became hypothyroid, TBAb and thyroid-stimulating antibodies (TSAb) were assessed, and thyroid $^{123}$I uptake and release after perchlorate administration were determined when possible.

**Methods**

**Subjects**

We prospectively studied 36 patients with Graves’ disease treated by radioiodine in our nuclear medicine department between 1996 and 2007 and followed up in our endocrinology clinic. All patients with Graves disease aged over 18 years old were included. Radioiodine was chosen because they did not tolerate antithyroid drugs (ATD) or because Graves’ disease relapsed. Patients with serious Graves’ orbitopathy were given corticosteroids before radioiodine, to avoid ophthalmopathy exacerbation as described in [13].

Patients received $^{131}$I at a dose calculated to deliver 80 Gy in order to obtain euthyroidism. A $^{123}$I dosimeter measured iodine fixation 3 and 24 hours after injection using parallel collimator. The dose was calculated according to the simplified Marinelli formula:

\[
\text{Therapeutic activity (MBq)} = \frac{\text{[absorbed dose (Gy) \times mass (g)]}}{0.042 \times \text{effective period (days)} \times \text{maximal uptake (\%)}].
\]

Free T4 (FT4) and TSH concentrations were measured just before radioiodine and every 3 months in the year following radioiodine treatment. In patients who developed precocious hypothyroidism, the TRAb stimulating activity and blocking activity were determined and $^{123}$I scintigraphy was performed in patients who developed precocious hypothyroidism.

**Hormone concentrations: free T4 and thyroid-stimulating hormone (TSH)**

FT4 was measured by a 2-step immunoextraction method using a kit from DiaSorin, Inc. (France); the normal range was 10.5–25.5 pmol/L. TSH was measured using an IMMULITE® 2000 kit (DPC Society, France) ($\text{SeF} < 0.01 \text{ mU/L}$, normal range, 0.4–3.6 mU/L).

**Antibodies titres: anti-thyroid peroxypase antibodies (TPOAb), anti-thyroglobulin antibodies (TGAb), anti-TSH receptor antibodies (TRAb)**

TPOAb concentration was measured using a kit from Brahms (Berlin, Germany); the normal range was $\leq 60 \text{ UI/mL}$. TGAb titre was measured using a kit from Sanofi Pasteur (France); the normal range was $\leq 50 \text{ UI/mL}$. TRAb titre was measured using a TBI kit (normal range $\leq 10\%$) and then a TRAK kit (normal range $< 2 \text{ UI/L}$) (both from Brahms). The TRAb titre measured using the TBIi and TRAK kits was expressed in relation to the normal range ($\times N$).

**Thyroid stimulating antibodies (TSAb) and thyroid blocking antibodies (TBAb)**

In patients who developed precocious hypothyroidism, the TRAb stimulating activity (TSAb; normal range $< 120\%$) and blocking activity (TBAb; normal range $> –10\%$) were determined by measuring cAMP in the JP cell line of transfected Chinese hamster ovary cells, which express high levels of the human TSH receptor [14,15].

**$^{123}$I scintigraphy**

$^{123}$I scintigraphy using an activity of 6.7 MBq was performed in patients who developed precocious hypothyroidism. In patients with fixation up to $10\%$, a perchlorate test was performed 3 hours after injection. The test was considered significantly positive when radioiodine uptake 1 hour after 1 g perchlorate (KClOH) ingestion decreased by more than $10\%$.

**Statistical analysis**

Fisher’s exact test was used to compare the qualitative parameters, and the Wilcoxon test to compare quantitative values between the 2 groups. We used a paired t test to compare the antibody titres before and after treatment in the combined group (more than 30 people). The increases in antibody titre from before to after treatment were compared using a paired Wilcoxon test in both groups (less than 30 people). A $\text{p value} < 0.05$ was considered significant. The data are expressed as mean ± standard deviation (SD), except for antibodies titres, which are expressed as mean ± standard error of the mean (SEM).

**Results**

**Thyroid status 1 year after treatment**

Thirty-six patients with Graves’ disease, aged 55.3 ± 14.6 years (range, 24–78 years), were included. Twenty-three patients developed hypothyroidism during the year following treatment (group A). Thirteen patients became euthyroid (2 patients) or relapsed hyperthyroidism (11 patients) comprised the comparison group (group B).

In group A, 15 patients were hypothyroid 3 months after radioiodine treatment, and all 23 patients after 6 months. Then levothyroxine therapy was begun. Levothyroxine could not be stopped in 22 of 23 (95\%) patients who remained hypothyroid. Hypothyroidism needing levothyroxine replacement was transient in only 1 patient, who could progressively stop this treatment after 6 months.

**Comparison of the initial characteristics in both groups: corticosteroid therapy (prescribed to prevent Graves’ orbitopathy aggravation) was used more frequently in patients who did not develop precocious hypothyroidism**

Four of the 36 patients had been treated previously by partial thyroidectomy. Eleven patients experienced Graves’ orbitopa-
thy (GO) before radioiodine treatment: 8 patients had a very mild stage, and 3 developed more serious GO and received prednisone (1 mg/kg/day) as recommended [13] begun the day before the $^{131}$I treatment and tapered over the following 3 weeks. Before $^{131}$I treatment, 25 patients were treated with antithyroid drugs (ATD): 17 patients with carbimazole, 3 with propylthiouracil, and 5 with benzylthiouracil. ATD were stopped 10 days before $^{123}$I scintigraphy. In 8 patients, radioiodine was the first therapy chosen. The mean functional thyroid mass was $49 \pm 37$ g (range, 10–158 g), and the patients received a mean dose of $^{131}$I of 480 ± 240 MBq (range, 129–1073 MBq). Initial thyroid concentration was 2,22-5,55 MBq/g (=60-150 microCi/g).

The characteristics of both groups are summarized in table I, and in (figures 1–3) (antibodies titers). The 2 groups did not differ significantly on age, sex, presence of a clinical ophthalmopathy, delay between diagnosis and radioiodine treatment, number of recurrences, treatment by ATD or by surgery before $^{131}$I, estimated thyroid mass before radioiodine treatment, or $^{131}$I dose (table I). Attendance for a serious GO that needed corticosteroid therapy during $^{131}$I treatment was more frequent in group B ($p = 0.0276$). Three of the 36 patients, all in group B, were given prednisone to prevent GO exacerbation. Notably, these 3 patients had high TRAb titres before (5.35N, 7.6N, and 17N) and 3 months after (109.5N, 6.3N, and 47N) radioiodine treatment. All three remained hyperthyroid after radioiodine treatment.

**Table I**

Comparison between the main initial characteristics of the 2 groups.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group A ($n = 23$)</th>
<th>Group B ($n = 13$)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) at diagnosis</td>
<td>56.9 ± 11.6</td>
<td>60.4 ± 15.7</td>
<td>NS</td>
</tr>
<tr>
<td>Age (years) at $^{131}$I</td>
<td>56.9 ± 11.6</td>
<td>60.4 ± 15.7</td>
<td>NS</td>
</tr>
<tr>
<td>Delay (years) between diagnosis and $^{131}$I</td>
<td>2.5 ± 0.9</td>
<td>2.4 ± 0.9</td>
<td>NS</td>
</tr>
<tr>
<td>Number of recurrences treatment before $^{131}$I</td>
<td>1.26 ± 0.9</td>
<td>0.9 ± 0.7</td>
<td>NS</td>
</tr>
<tr>
<td>Antithyroid drugs</td>
<td>17/23</td>
<td>8/13</td>
<td>NS</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>0/23</td>
<td>3/13</td>
<td>0.0276</td>
</tr>
<tr>
<td>Partial surgery</td>
<td>3/23</td>
<td>1/13</td>
<td>NS</td>
</tr>
<tr>
<td>Orbitopathy</td>
<td>6/23</td>
<td>5/13</td>
<td>NS</td>
</tr>
<tr>
<td>Doses (MBq)</td>
<td>473 ± 238</td>
<td>492 ± 253</td>
<td>NS</td>
</tr>
<tr>
<td>Mass (g)</td>
<td>43.8 ± 31.3</td>
<td>60.4 ± 46.4</td>
<td>NS</td>
</tr>
</tbody>
</table>

Group A = patients who developed precocious hypothyroidism. Group B = patients who did not developed precocious hypothyroidism. Data are expressed in mean ± standard deviation (SD).

Anti-TSH receptor antibodies (TRAb) titres rose significantly 3 months after radioiodine treatment in both groups, but the titres did not differ significantly between the 2 groups before or after radioiodine treatment

In the whole population, the mean TRAb titre increased significantly 3 months after treatment ($p = 0.0146$). TRAb titre increased in 27 patients, was unchanged in 2 patients, and decreased in 7 patients.

In group A, the mean TRAb titre also increased significantly 3 months after radioiodine treatment ($p = 0.0016$) (figure 1). TRAb increased in 16 patients, remained unchanged in 1 patient, and decreased in 6 patients. After 12 months, TRAb titre diminished in 93% of patients and even disappeared in 35% of patients. The mean concentration was 5 ± 2N (range, 0.5–15N).

In group B, the mean TRAb titre also increased significantly 3 months after treatment ($p = 0.0098$) (figure 1). TRAb titre increased in 11 patients, decreased in 1 patient, and remained unchanged in 1 patient.

TRAb titre did not differ significantly between groups A and B before treatment or 3 months after treatment (figure 1). The extent of the increase in TRAb titre did not differ significantly between the groups A and B.

A thyroid blocking antibodies (TBAb) activity was detected in 13 hypothyroid patients

When hypothyroidism occurred, significant TSAb activity was detected in 13 of the 23 (56%) patients. Four patients had
significant TSAb activity only, 6 patients had significant TBAb activity only, and 7 patients had significant activities of both antibodies. In 2 patients, because of a very high stimulating activity, it was impossible to determine whether there was an associated blocking activity. Four patients had no TBAb activity, and their TSAb activity was just in normal range (between 100 and 115%). Notably, TBAb activity was detected only in patients who had a significantly increased TRAb titre (in 11 of 13 patients, 85%). Conversely, blocking activity was present in 11 of the 16 (69%) patients whose TRAb titre increased. In 1 patient, the hypothyroidism was transient. Moderate TSAb activity and a nearly significant TBAb activity were detected 3 months after radioiodine treatment. TBAb activity then increased, and TSAb activity decreased. Finally, when TBAb activity decreased, the patient recovered normal thyroid function 1 year after treatment.

Anti-thyroid peroxidase antibodies (TPOAb) concentration 3 months after radioiodine treatment was significantly higher and remained elevated in hypothyroid patients.

In all patients just before treatment, the mean TPOAb concentration increased significantly to 3 months after treatment ($p < 0.0001$). In group A, the mean TPOAb concentration also increased significantly ($p < 0.0001$, figure 2). Notably, TPOAb concentration increased in every patient. However, in group B, the mean TPOAb concentration increased moderately but nonsignificantly 3 months after radioiodine treatment (figure 2). The extent of the increase in TPOAb concentration did not differ significantly between groups. The TPOAb concentration did not differ between groups before radioiodine treatment (figure 2) but was significantly higher 3 months after treatment in group A than in group B ($p = 0.0112$ (figure 2).

Anti-thyroglobulin antibodies (TGAb) concentration was significantly higher in hypothyroid patients before and 3 months after radioiodine treatment. The increase in TGAb concentration was significant only in hypothyroid patients

In all patients, the mean TGAb concentration increased significantly 3 months after treatment ($p < 0.0141$). In Group A, TGAb was undetectable (< 50 UI/mL) in only 8 of the 23 (34%) patients. When hypothyroidism occurred, the TGAb concentration increased significantly ($p = 0.0305$) (figure 3). In contrast, in Group B, the TGAb concentration before radioiodine treatment was undetectable in 90% of the patients. TGAb concentration increased non-significantly 3 months after treatment (figure 3).

The magnitude of the increase in TGAb concentration did not differ between the groups. TGAb concentration was significantly higher in group A than in group B before ($p = 0.0024$) (figure 3) and 3 months after radioiodine ($p = 0.0024$) treatment (figure 3).

Scintigraphic results

In group A, a low $^{123}$I uptake (< 10%) was observed in 13 of 16 (81%) patients when hypothyroidism occurred. In all patients with a measurable TBAb titre, $^{123}$I fixation was < 6%. In 3...
patients, fixation reached 12%, but the perchlorate test was negative. These results discounted the role of acquired iodide impairment.

**Discussion**

Radioiodine therapy is considered a safe and rapidly effective treatment for hyperthyroidism related to Graves’ disease. Mild anterior cervical neck pain and transient exacerbation of thyrotoxicosis, caused by radiation thyroiditis, can occur precociously [1]. Hypothyroidism results from the destruction of the parenchyma function by radiations and development of fibrosis. However, some patients exhibit a precocious transient hypothyroidism usually in the first 6 months after radioiodine intake [5]. Only a few studies have focused on the mechanisms responsible for precocious hypothyroidism, commonly referred to as persistent TSH suppression or transient thyroid injury [1]. Early exacerbation of thyrotoxicosis followed by transient hypothyroidism suggests subacute radioiodine-induced thyroiditis [1]. Some authors have suggested the involvement of immunologic factors such as changes in the conformation of TRAb [9,10]. We found that TRAb titre increased considerably in the 3 months following radioiodine treatment in patients with Graves’ disease, as documented previously [10,16–18]. This well known phenomenon is thought to relate to thyroid antigens, such as TSH receptor molecules, released from the disrupted follicular cells and to the subsequent boosting of the autoimmune response [6,7]. We observed this augmentation in 27 of 36 patients (76%), which is comparable to previous studies [18–20]. In our study, TRAb titre before and 3 months after radioiodine was notably higher in patients who developed hypothyroidism, although this difference was not statistically significant. Serum TRAb level increased more in patients who became hypothyroid after a 1-year follow-up in the study by Andrade et al. [21]. TPOAb and TGAb concentrations increased more in patients who became hypothyroid. These patients had constant and significant increase in TPOAb concentrations, whereas the concentrations increased non-significantly or inconsistently in patients who did not become hypothyroid. This precocious elevation in the concentration of TPOAb has been reported in smaller series [6,10]. We wondered whether the appearance of these antibodies would correlate with the occurrence of hypothyroidism caused by the effect of impaired thyroperoxidase activity on iodide organization. For this reason, 123I scintigraphy was performed when hypothyroidism occurred. An uptake > 10% was found in 3 patients, and the perchlorate test was negative in all patients, suggesting no involvement of an acquired iodide organization disorder that would have impaired hormonal biosynthesis. TPOAb acts principally in complement activation and NK lymphocyte recruitment for antibody-dependent cellular cytotoxicity [22]. Thus, TPOAb probably does not play a functional role in the development of hypothyroidism, and the relapse of patients might reflect serious tissue damage caused by radioiodine, which leads to an intensive inflammatory reaction. TGAb concentration was significantly higher after radioiodine treatment only in the hypothyroid group. Similar results were found by Chiovato et al in a study of 31 patients [6]. Taken together, these data suggest that increased antibody levels (TPOAb, TGAb, and less obviously TRAb) in patients who became early hypothyroid reflect serious radioinduced thyrocyte lysis, which releases a large amount of thyroid antigens. This early radioinduced thyroiditis leads to precocious hypothyroidism.

The TGAb level before radioiodine treatment might be informative because it was significantly higher before the treatment in patients who developed precocious hypothyroidism. In addition, TGAb was undetectable in 90% of patients who did not develop hypothyroidism. Interestingly, in a retrospective study, Bringmann et al reported a similar result that the main predictors of hypothyroidism after radioiodine treatment are positive titre of both TPOAb and TGAb; the positive predictive values were 79.5 and 91.6 respectively [4]. However, in our study, TPOAb concentration was similar before radioiodine treatment in the two groups. TGAb concentration before radioiodine treatment may be of interest because a high concentration before treatment might predict the development of precocious hypothyroidism. In the 23 patients who became hypothyroid, TBAb activity was found in 13 (56%), TSAb activity in 13 (56%), and both TBAb and TSAb activities in 4 (17%). Interestingly, TBAb activity was detected mainly in patients whose TRAb titre increased in 11 of 13 patients with significantly elevated TBAb titre. In addition, blocking activity was present in 11 of 16 (69%) patients whose TRAb titre increased. Thus increased TRAb titre is associated with blocking activity in most patients. One may hypothesize that TBAb is involved in the development of precocious hypothyroidism. Moreover, in 1 patient, hypothyroidism progressed while TBAb activity decreased, suggesting a crucial role of TBAb in this transient hypothyroidism. This phenomenon has been described previously [6,9–11]. Kung et al compared 12 euthyroid patients with 11 patients who developed a transient hypothyroidism after radioiodine treatment and found similar increases in TSAb activity in the 2 groups but a significant increase in TRAb titre and TBAb activity only in patients with transient hypothyroidism [12]. This suggests that the blocking activity can rarely explain the appearance of early hypothyroidism and its progressive disappearance at recovery of euthyroidism.

Interestingly, we found that corticosteroid treatment for moderate GO was significantly associated with the absence of precocious hypothyroidism. Corticosteroid therapy was begun just before radioiodine treatment to avoid aggravating the GO [13]. In the hypothyroid group, no patient needed corticoster-
oid therapy for GO. However, it has been shown that corticosteroids do not influence later thyroid status [6,23], which seems to be contradictory. An alternative explanation is that attendance for moderate or severe GO (rather than corticosteroid treatment itself) is related to later thyroid status outcome. In our study, the 3 patients with the more severe GO (who needed corticosteroid prevention) stayed hyperthyroid and had very high TRAB titres before and after treatment. Severe GO is related to high TSAb activity [24]. TSAb and TRAB levels are higher in GO that is resistant to treatment and can remain high despite corticosteroid therapy [25]. Thus, the absence of precocious hypothyroidism is more likely to be related to moderate or severe Graves’ ophthalmopathy (needing prevention by corticosteroid) than to the prednisone treatment itself. High TSAb activity probably contributes to hypothyroidism relapse. Finally, we found no significant difference between the 2 groups on age, sex, presence of a clinical ophthalmopathy (without specifying GO severity), delay between diagnosis and radioiodine treatment, number of recurrences, treatment by ATD or by surgery before 131I, 131I dose, and estimated thyroid mass before radioiodine treatment. This last point is noteworthy because we found no relationship between the estimated thyroid mass before treatment and thyroid status outcome. In contrast, Chiovato et al found that pre- and post-therapeutic ultrasonographic thyroid volume was the best predictor of thyroid function 1 year after treatment [6]. The difference between our study and that by Chiovato et al probably relates to different methods of evaluating thyroid mass. We estimated functional thyroid mass using 123I scintigraphy, whereas they used ultrasonographic morphological measurements to determine thyroid mass. They considered the whole thyroid mass, including the non-functional areas, whereas we included only the functional tissue in our analysis.

Conclusion

Precocious hypothyroidism is observed frequently after radioiodine therapy for Graves’ disease, even with a 131I dose calculated to obtain euthyroidism. A high TgAb concentration before radioiodine treatment correlates with the occurrence of early hypothyroidism. Patients who develop precocious hypothyroidism 3 months after radioiodine treatment have significantly higher TPOAb and TgAb concentrations, suggesting more severe tissue damage and antigen release. Radioiodine-induced thyroiditis leading to a reduction in the amount of functional thyroid tissue seems to be the main mechanism responsible for the pathogenesis of precocious hypothyroidism. Transient hypothyroidism directly due to TRAb blocking activity remains rare but conceivable as a cause, whereas acquired organification disorder does not appear to be involved in the development of precocious hypothyroidism. However, current radioiodine therapy strategy in much centres aims at eradicating hyperthyroidism rather than at restoring euthyroidism.

Conflicts of interest : None.

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