NON-TOXIC GOITRE

Dyshormonogenesis

By

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ABSTRACT

Among 50 consecutive patients operated on for non-toxic goitre, ten had an iodine dynamic pattern compatible with dyshormonogenesis, i.e. a high absolute iodine uptake (AIU) in the thyroid gland or a positive perchlorate discharge test. Extensive investigations of the ten patients were performed including chromatography of the serum, urine and thyroid gland digest.

Six of the ten patients had dyshormonogenesis. Two patients had an iodine organification defect as part of Pendred's syndrome. In another a coupling defect was found. One patient differed in only two respects from the patients with simple iodine deficiency; the plasma inorganic iodine (PII) was found to be normal and the patient became hypothyroid soon after operation. A patient had recurrent goitre and a raised serum TSH in spite of an elevated serum thyroxine and normal TBG. The defect in this case could be a reduced cellular sensitivity to thyroxine which included the pituitary gland. Furthermore, a case of diffuse hyperplastic parenchymatous goitre was found.

No case of a trapping defect or deiodinase defect was found. All the patients had elevated non-butanol extractable $^{125}\text{I}$ (NBEI).

Dyshormonogenesis is a term used when the thyroid gland fails to produce a normal amount of hormones due to an inborn defect in hormone synthesis. Whatever the cause of the defective hormone production, an increased TSH secretion occurs and gives rise to a compensatory increase in the activity of the thyroid and goitre develops.

In 118 consecutive patients with non-toxic goitre we found 17 patients (14.4 %) with either a high absolute iodine uptake (AIU) in the thyroid gland and a normal or low PBI or with perchlorate discharge of iodide from the gland; thus these patients presented evidence suggestive of at least functional dyshormonogenesis (Agerbæk & Jensen, to be published). In 50 patients operated on for non-toxic goitre 10 had findings suggesting dyshormonogenesis, but in only 6 was this the final diagnosis. In the present paper extensive investigations are presented concerning these six patients. Furthermore, chromatography of the digested thyroid tissue from 5 patients without any thyroid disease has been included.

**METHODS**

The thyroid clearance of iodine (th. cl.), plasma inorganic iodide (PII), renal clearance of iodide (ren. cl.) and AIU were measured according to Wayne et al. (1964). Our normal value for th. cl. is 31.1 ± 2.4 ml/min, for PII 0.123 ± 0.01 µg/100 ml, for ren. cl. 30 ± 1.7 ml/min, and for AIU 2.1 ± 0.14 µg/h (Mean ± SEM) (Agerbæk & Jensen, to be published). After the gland-uptake measurement at hour 2 1/2, 500 mg of potassium perchlorate was given orally, and radioactivity over the thyroid gland was continuously recorded for half an hour. A fall in radioactivity greater than 15 % of the starting values was considered abnormal.

Seven days before operation, the patients were given a tracer dose of Na125I orally, and the thyroid uptake, [125I]PBI, [125I]NBEI and total plasma radioactivity measured daily. The activity of the tracer dose was estimated from a thyroid-uptake measurement of 131I, with the aim of producing a concentration of 1–2 µCi/g tissue in the thyroid gland at the time of operation. Immediately after resection, the thyroid tissue was examined for its content of 125I labelled amino acids and 125I concentration. Digestion and chromatography of the thyroid gland tissue for iodinated amino acids were performed using a procedure which has been described previously (Agerbæk 1972).

Thyroid tissue, 1–2 g, was removed from 5 patients without any thyroid disease during mediastinoscopy or at operation 7 days after a tracer dose of Na125I had been given. These patients had the following diagnoses: Boeck's sarcoidosis, tumour of the lung, pulmonal infiltrates (two), and parathyroid adenoma. The last patient had a PBI of 8.5 µg/100 ml but a normal T3 Sephadex uptake and serum cholesterol. On microscopy, all 5 biopsies showed normal thyroid tissue.
The ability to deiodinate iodothyrosines was assessed by giving the patients about 30 µCi $[^{125}\text{I}]$MIT orally and collecting urine samples for the next 6 hours. Radioactivity was measured and chromatography done to evaluate the excretion of unaltered $[^{125}\text{I}]$MIT. N-butanol-acetic acid-water (12:3:5) was used as the chromatography solvent. $[^{125}\text{I}]$MIT recovery by this procedure is 100% when chromatographing $[^{125}\text{I}]$MIT added to urine 7 hours before application to chromatography paper.

Chromatography of the serum for radioactive labelled compounds was performed by taking 10 ml of serum at various time intervals after the tracer dose Na$^{125}$I was given. To concentrate iodo-amino acids the serum was adsorbed on Dowex I–II, 100–200 mesh, in the anion form at a pH of approximately 9. The resin was placed in a vessel and washed with water until the effluent had a pH of 7. Iodinated compounds were eluted with 25 ml 99% acetic acid, and evaporated to dryness. The residue was dissolved in methanol-acetic acid and applied to Whatman 3 MM paper for ascendent chromatography in n-butanol-acetic acid-water (12:3:5) and/or n-butanol-ethanol-ammonia 0.4 n (15:3:6). Using this procedure recovery of the individual compounds MIT, DIT, T$_3$ and T$_4$ were found to be the same, and hence the relative distribution should be considered as valid.

$[^{125}\text{I}]$PBI was measured as trichloracetic acid precipitable radioactivity and $[^{125}\text{I}]$NBEI by the method of De Groot & Stanbury (1959). PBI was measured using an autoanalyser technique (normal range 3.5–7.5 µg/100 ml). T$_3$ Sephadex uptake by the method of Hansen (1969) (normal range 4.4–6.8%). Serum T$_4$ was measured by a modification of Murphy’s technique; in this modification the pooled serum was deprived of thyroxine before adding radioactive thyroxine, and furthermore separation of the free- and protein-bound T$_4$ was achieved on albumin coated charcoal. The normal range is 4.8–10.6 µg T$_4$/100 ml. Thyroxine binding globulin (TBG) was measured by the method of Nielsen et al. (1972) (normal range 68–140 arbitrary units).

**CASE HISTORIES**

**Case 1.** — 21-year old woman whose sister has a goitre and is hard of hearing. She, herself, has been deaf from birth, and since the age of 6 has had a goitre. A clerical examination had been passed with distinction. At the age of 8 she did not have any hypothyroid symptoms, the skin was normal, and she behaved normally. The bone age was normal, but she was 8 cm shorter than the average height. PBI of 1.0 and 1.9 µg/100 ml were found, and since that time she has received thyroid hormone treatment. This treatment was discontinued one month before the laboratory measurements shown in the tables. No recurrence of goitre noted so far, i.e. 1 1/2 years after operation and during treatment with thyroid hormones. The thyroid gland was multinodular, and only connective tissue was found between the nodules. No signs of thyroiditis were found at microscopy and no circulating thyroid antibodies were detected.

**Case 2.** — 24-year old woman whose sister is deaf and has a goitre and who has a deaf brother with no goitre. She, herself, was deaf from birth and a goitre was noted since the age of 10. She was treated with thyroid hormones from her 13th to the 18th year because of euthyroid goitre and again during
pregnancy at the age 23 years. Treatment with thyroid hormones ceased 8 months before the laboratory investigation. The thyroid gland then was large, multinodular and only connective tissue was found between the nodules. Goitre has not recurred since 3 years after the operation during which time the patients has been treated with thyroid hormones.

Case 3. – 19-year old woman with an increasing goitre since the age of 12 and rapid growth of the goitre since normal delivery one year before the investigation. Her mother had been operated on three times because of goitre. For many years she had slept 14 hours a day and for half a year had been constipated. Menstruation and hearing were normal. Clinically she was slightly hypothyroid, appeared lethargic and responded slowly. No thyroid antibodies

![Fig. 1.](image)

Thyroid gland digest chromatography of case No. 3 with the coupling defect. At the application site of the chromatogram digest (upper part) and standard DIT, MIT, I⁻, T₄ and T₃ (lower part) overlaps. At each end of the chromatogram, a piece of tape has produced an artifact. The figures at the bottom indicate the relative distribution of radioactivity in per cent of total radioactivity of the chromatogram. The [¹²⁵I]MIT/DIT ratio is high and very small amounts of [¹²⁵I]thyronines are found.
were found in the blood. The thyroid gland was diffusely enlarged, rich in
vessels and microscopy showed a considerable hyperplasia of the thyroid tissue.
Chromatography of the thyroid tissue is shown in Fig. 1. Since operation
3 years ago the patient has been treated with thyroid hormones. She has been
euthyroid and goitre has not recurred.

Case 4. – 42-year old man whose sister and father’s sister have goitres. At
operation his goitre was large and very soft. Histological examination of the
gland showed colloid tissue with poorly demarked adenomata. No thyroid

Fig. 2.
Diffuse, hyperplastic, parenchymatous goitre. Case No. 6. A (100 ×): microfollicular
and solid proliferation of columnar epithelium with papilliferous processes. Small
lymphocytic infiltrations in the stromal tissue. B (300 ×): hyperplastic follicular epi-
thelium with fine granular, cosinophilic cytoplasm. Sparce colloid.

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antibodies were found in the blood. Although about 19 g of thyroid tissue was left at operation, the patient developed hypothyroid symptoms during the following 6 months. The PBI fell to 1.2 μg/100 ml, the thyroid clearance to 14 ml/min, and the AIU to 1.0 μg/h. Substitution therapy was then started with thyroid hormones and he has since felt well and no recurrence of goitre has occurred during the past 3 years.

Case 5. – 42-year old woman who has 8 goitrous relatives in five generations. The patient has had a goitre since early childhood. Resection of the goitre was performed when she was 16 and again at the age of 31. On admission she was found to be clinically euthyroid and she had normal hearing. No thyroid antibodies were found in the blood. She did not take contraceptive agents or any other drugs. A large multinodular goitre with no signs of hyperactivity at microscopy was present. After operation about 20 g of the thyroid gland remained. No recurrence of the goitre has occurred one year after operation.

Case 6. – 49-year old woman with a goitrous sister and cousin. She had had an increasing goitre for 6 years and during the same period suffered from heat intolerance, nervousness, a tendency to tachycardia and a feeling of pressure in the neck. Her body weight remained constant. Clinically, she was judged to be euthyroid, but she had slight exophthalmos. The gland was diffusely enlarged and at microscopy the characteristic picture of a diffuse hyperplastic.

Fig. 3.
Thyroid gland digest chromatography of case No. 6 with the diffuse, hyperplastic, parenchymatous goitre. Large amounts of [125I]thyronines are obviously found here.
parenchymatous goitre was found (Fig. 2). Circulating antibody against thyroid extract was positive in a low titre, 64, but negative against thyroglobulin. Correspondingly a few lymphocyte foci were found at microscopy of the gland. Chromatography of the thyroid digest is given in Fig. 3. About 17 g of the thyroid tissue was left at operation, but a few months later the patient developed hypothyroidism clinically and a thyroid clearance of 9 ml/min, an AIU of 0.5 µg/h and a PBI of 1.9 µg/100 ml were found. She has since been euthyroid on treatment with thyroid hormones and there has been no recurrence of the goitre for 4 years.

RESULTS

Relevant laboratory findings in the six patients are listed in Tables 1, 2 and 3.

Table 1.
Thyroid parameters in six non-toxic goitre patients with a high AIU or a positive perchlorate iodide discharge.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age and sex</td>
<td>21 F</td>
<td>24 F</td>
<td>19 F</td>
<td>42 M</td>
<td>42 F</td>
<td>49 F</td>
</tr>
<tr>
<td>Thyr. clear. ml/ml</td>
<td>20</td>
<td>45</td>
<td>954</td>
<td>119</td>
<td>157</td>
<td>430</td>
</tr>
<tr>
<td>PII µg/100 ml</td>
<td>0.130</td>
<td>0.090</td>
<td>0.048</td>
<td>0.092</td>
<td>0.080</td>
<td>0.053</td>
</tr>
<tr>
<td>AIU µg/h</td>
<td>1.56</td>
<td>4.10</td>
<td>27.2</td>
<td>6.55</td>
<td>7.5</td>
<td>13.8</td>
</tr>
<tr>
<td>Renal clear. ml/min</td>
<td>36</td>
<td>27</td>
<td>35</td>
<td>37</td>
<td>35</td>
<td>45</td>
</tr>
<tr>
<td>Perchlorate discharge</td>
<td>65</td>
<td>31</td>
<td>119</td>
<td>12</td>
<td>64</td>
<td>50</td>
</tr>
<tr>
<td>%/min</td>
<td>1.27</td>
<td>1.27</td>
<td>1.27</td>
<td>1.27</td>
<td>1.27</td>
<td>1.27</td>
</tr>
<tr>
<td>1.27 I excretion µg/24 h</td>
<td>119</td>
<td>12</td>
<td>64</td>
<td>50</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td>1.27 I conc. of thy. gl. µg/g</td>
<td>8</td>
<td>100</td>
<td>22</td>
<td>202</td>
<td>402</td>
<td>126</td>
</tr>
<tr>
<td>Weight of thy. gl. g</td>
<td>130</td>
<td>355</td>
<td>188</td>
<td>214</td>
<td>87</td>
<td>88</td>
</tr>
<tr>
<td>PBI µg/100 ml</td>
<td>1.9</td>
<td>2.8</td>
<td>1.2</td>
<td>4.4</td>
<td>11.4</td>
<td>3.6</td>
</tr>
<tr>
<td>T3 sephadex uptake %</td>
<td>5.6</td>
<td>3.2</td>
<td>5.8</td>
<td>6.2</td>
<td>5.9</td>
<td>8.6</td>
</tr>
<tr>
<td>Cholesterol mg/100 ml</td>
<td>150</td>
<td>333</td>
<td>159</td>
<td>252</td>
<td>264</td>
<td>230</td>
</tr>
<tr>
<td>BMR ± %</td>
<td>-3</td>
<td>-5</td>
<td>-12</td>
<td>-2</td>
<td>+8</td>
<td>+17</td>
</tr>
<tr>
<td>[125I]MIT excretion % dose/6 h</td>
<td>0.8</td>
<td>1.0</td>
<td>0.6</td>
<td>1.1</td>
<td>0.3</td>
<td>0.4</td>
</tr>
</tbody>
</table>

a) Mean of 3 measurements.

b) Left lobe.

c) Right lobe.

d) Mean of 6 measurements.
Table 2.

Measurements of thyroid gland uptake and various aspects of the plasma $^{125}$I after an oral dose of Na$^{125}$I. The $[^{125}]$PBI and $[^{125}]$NBEI were measured every 24 h for 5 to 7 days. The figures listed under chromatography of serum give % of total radioactivity on the chromatograms.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{125}$I uptake in the Thygr. gland % of dose</td>
<td>24 h</td>
<td>26</td>
<td>58</td>
<td>78</td>
<td>53</td>
<td>43</td>
</tr>
<tr>
<td>$[^{125}]$PBI % of dose/l</td>
<td>144 h</td>
<td>14</td>
<td>45</td>
<td>79</td>
<td>54</td>
<td>40</td>
</tr>
<tr>
<td>$[^{125}]$NBEI × 100 % max.</td>
<td>0.517</td>
<td>0.278</td>
<td>0.072</td>
<td>0.028</td>
<td>0.044</td>
<td>1.035</td>
</tr>
<tr>
<td>Time after tracer dose h</td>
<td>144</td>
<td>48</td>
<td>144</td>
<td>24</td>
<td>24</td>
<td>48</td>
</tr>
<tr>
<td>Chromatography of serum solvents</td>
<td>a</td>
<td>b</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>$[^{125}]$T$_4$</td>
<td>96</td>
<td>46</td>
<td>70</td>
<td>100</td>
<td>74</td>
<td>81</td>
</tr>
<tr>
<td>$[^{125}]$T$_3$</td>
<td>14</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$[^{125}]$MIT + DIT</td>
<td>14</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$[^{125}]$Origin</td>
<td>14</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Solvents
  a: n-butanol-acetic acid-water (12:3:5).
  b: n-butanol-ethanol-ammonia 0.4 N (15:3:6).

DISCUSSION

Among the 50 patients investigated ten actually had an elevated absolute iodine uptake in the thyroid gland or a positive perchlorate discharge test. In the supplementary investigations four patients were shown not to have a dys-hormonogenesis in the general sense: one had Hashimoto's thyroiditis, and another one had a solitary "warm" nodule in the thyroid gland. The third patient turned out to be pretoxic, and the last patient had a simple iodine deficiency.

None of the six patients presented here had an iodide trapping defect since all of them concentrated radioactive and stable iodine in their thyroid glands, and indeed to a greater extent than normal.

Defects in dehalogenase were also not present. In Table 1 it can be seen that the excretion of $[^{125}]$MIT during the 6 hours after the patients had received the $[^{125}]$MIT dose was 1.1 % or less of the dose given. McGirr et al. (1959) found the normal excretion to be up to 6 % and this included the MIT derivates.
Table 3.
Thyroid gland chromatography 7 days after in vivo $^{125}$I labelling. The figures indicate per cent of total radioactivity on the chromatogram (mean of duplicate estimations). Origin (Or) includes all radioactivity from application site to the DIT band.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>Normal thyroids mean of 5 ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid tissue</td>
<td>Multi-nodular</td>
<td>Multi-nodular</td>
<td>Diffuse</td>
<td>Diffuse</td>
<td>Left lobe</td>
<td>Right lobe</td>
<td>Diffuse</td>
</tr>
<tr>
<td>Or</td>
<td>7.4</td>
<td>6.1</td>
<td>4.7</td>
<td>9.1</td>
<td>18.0</td>
<td>13.6</td>
<td>8.2</td>
</tr>
<tr>
<td>DIT</td>
<td>16.2</td>
<td>20.1</td>
<td>16.3</td>
<td>26.5</td>
<td>25.3</td>
<td>19.2</td>
<td>23.2</td>
</tr>
<tr>
<td>MIT</td>
<td>49.0</td>
<td>60.5</td>
<td>73.8</td>
<td>54.4</td>
<td>48.6</td>
<td>59.2</td>
<td>38.7</td>
</tr>
<tr>
<td>I$^-$</td>
<td>13.0</td>
<td>5.8</td>
<td>3.4</td>
<td>5.7</td>
<td>5.6</td>
<td>5.1</td>
<td>7.3</td>
</tr>
<tr>
<td>T$_4$</td>
<td>12.7</td>
<td>3.9</td>
<td>1.3</td>
<td>3.2</td>
<td>1.9</td>
<td>1.9</td>
<td>17.4</td>
</tr>
<tr>
<td>T$_3$</td>
<td>1.3</td>
<td>2.4</td>
<td>0.5</td>
<td>0.8</td>
<td>0.4</td>
<td>0.5</td>
<td>3.6</td>
</tr>
</tbody>
</table>

$^{125}$I conc.
left lobe/right lobe 5.4/1
found on the chromatogram. In no case did we find radioactivity at other sites than at the corresponding to iodide and MIT on the chromatogram apart from a very small amount close to the front.

Two patients, cases 1 and 2, had a perchlorate induced discharge of iodide (Table 1) suggesting a defect in the organification of iodide. Both patients had goitres from early childhood, and both showed perception deafness. PII values were normal and thus the positive perchlorate discharges could not be results of iodide contamination. Both glands were multinodular and microscopy showed no signs of thyroiditis. The defective organification in case 1 was pronounced with a perchlorate discharge of 65%/h. However, organified iodide was quickly metabolised as shown by the high [125]I PBI (Table 2). [125]NBEI, a measure of non-metabolic active iodine in the serum, was also high, i.e. 58% of [125]PBI 48 h. The proteins or peptides associated with this iodine are not characterized in the present study, but serum chromatography revealed only 125I corresponding to T3 + T4. The concentration of 127I in the thyroid gland was extremely low, 8 μg/g wet tissue, apparently due to treatment of the patient with thyroid hormones for 13 years as well as leakage of iodide and non-metabolic active iodinated proteins from the thyroid gland. As in cases with simple iodine deficiency, a high [125]MIT/DIT ratio was found. Case 2 differs from the preceding patient in having a considerably higher but still abnormal iodine concentration in the thyroid gland probably due to the less pronounced organification defect and intermittent hormonal treatment. In this case a normal concentration of [125]T4 + T3 in the thyroid gland and, as in case 1, a high [125]MIT/DIT ratio were found. Serum chromatography (Table 2) revealed a high proportion of 125I remaining at the origin of the chromatograms and significant amounts of [125]tyrosines, which suggests secretion from the thyroid of non-metabolically active components. In case 1 the [125]NBEI was even higher than in case 2, but in spite of this only iodothyronines were found on chromatography of the serum. It is not likely that the high [125]NBEI in case 1 had disappeared during the laboratory procedure since recovery of radioactivity in the various steps before serum chromatography was very similar in the two cases. In conclusion, the [125]NBEI in case 1 must represent iodothyronines firmly bound to serum proteins, but which could be eluted as free iodothyronines by iced acetic acid in the Dowex column. Both patients had an iodide organification defect and impaired hearing. They belong to that group of patients classified as having Pendred's syndrome. They are different, however, in their aberrant organic binding, as reflected by serum chromatography.

Case 3 had an extremely high clearance of iodide and an AIU thirteen times greater than our normal mean value. The percentage tracer uptake in the gland was high, and remained high during the five days in which it was measured. Correspondingly, a low [125]I PBI was found in the serum. The
ratio of $[125I]$MIT to DIT in the thyroid was 4.5 which is higher than in any other case, and the concentration of $[125I]$thyronines was very low (Table 3). In spite of the huge amounts of iodide taken up by the thyroid, 0.6 mg/24 h, the iodine concentration in the thyroid was very low, which means that large amounts of iodine quickly re-circulated in and out the gland. This iodine must be organically bound after entering the gland since perchlorate did not discharge it. The deiodinase activity was found to be normal by the $[125I]$MIT test (Table 1), and the deiodinase enzyme capacity seemed large enough to prevent the secretion of MIT and DIT from the thyroid, as seen by the finding of only iodothyronines on chromatography of the serum. The large leakage of inorganic iodine from the thyroid gland presumably stems from this source. The low PII and low iodine excretion in the urine points to iodine deficiency, but this cannot be the only explanation for all the pathological findings. Especially the very high AIU, the very low iodothyronine-concentration in the thyroid and the hypothyroid state of the patient are consistent with a defective coupling of iodotyrosines to iodothyronines.

In case 4 the PII was found to be 0.092 µg/100 ml – a normal value – but apart from this all the other parameters measured did not differ from the values of a larger group of non-toxic goitre patients with simple iodine deficiency (Agerbæk & Jensen, to be published). The PII of this patient could be spuriously elevated because of an unusual high dietary intake of iodine on the day of measurement. On the other hand none of 15 patients with simple iodine deficiency and a normal AIU investigated by us became hypothyroid after operation as did case No. 4.

Case 5 was clinically euthyroid and by all parameters except for a high PBI, a total serum $T_4$ of 18.0 µg/100 ml, and a high free serum $T_4$ of 122 pmol/l. After resection of the goitre these parameters were still elevated. The $T_3$ Sephadex uptake was normal and TBG concentration was also normal, 118 units. Serum TSH was elevated both before and after operation, in spite of a high serum $T_4$. Further information on this patient and her family will be published later (Agerbæk & Weeke). An elevated cellular resistance to thyroxine, which included the pituitary gland, seemed to be operative, but the primary defect in this case has not been clarified.

The goitre of case 6 is a type very infrequently seen in Danmark. Guinet (1963) described the characteristic microscopic picture of the gland, and furthermore he found a normal BMR, serum cholesterol and PBI, and a high $[131I]$PBI in the serum of these patients. Treatment with triiodothyronine suppresses $[131I]$uptake in the thyroid gland and causes disappearance of the goitre.

Our patient had menopausal symptoms during some years, she was nervous but was judged to be euthyroid. The PBI was low. Chromatography of the thyroid digest revealed a radioactive iodothyronine concentration much greater than our normal mean value. The $[125I]$NBEI reached a maximum at 48 h and
thereafter a steady fall was seen, so that at 144 h it was only 13 % of the $^{125}$I as iodothyronines. The PII was low. The gland took up about 336 µg of iodide per 24 h. Iodine excretion in the urine was 60 µg. Assuming a steady state, about 276 µg of iodine must circulate in and out of the gland – possibly a little less because of extra-renal excretion.

All the six patients had high values of $[^{125}$I]NBEI (Table 2), the maximal values at various days after administration of the tracer dose being 35-78 % of $[^{125}$I]PBI. In spite of this, serum chromatography revealed iodinated components other than $[^{125}$I]$T_3$ and $T_4$ in only a few cases. High values of NBEI in the serum are found in a variety of thyroid disorders (Furth et al. 1970) and therefore the plasma iodoprotein disorder should not be considered as a separate entity.

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