TREATMENT OF EIGHT CASES OF HYPERTHYROIDISM WITH COBALTOUS CHLORIDE

Enrique Pimentel-Malaussena, M.D., Marcel Roche, M.D.
and Miguel Layrisse, M.D., Caracas, Venezuela

Kriss, Carnes, and Gross \(^1\) reported in 1955 the development of thyroid hyperplasia in four children and one adult receiving cobaltous chloride by mouth in doses ranging from 2.8 to 3.9 mg per kilogram per day. In three subjects, in whom radioiodine \((I^{131})\) studies were done, it was found that thyroid \(I^{131}\) uptake was markedly depressed. Jaimet and Thode \(^2\) have thrown serious doubts on those findings, since they were unable to demon-

Assistant Professor of Clinical Medicine, Universidad Central (Dr. Pimentel-Malaussena); Director, Instituto de Investigaciones Médicas (Dr. Roche); and Director, Research Department, Banco de Sangre Municipal (Dr. Layrisse).

Eight patients with hyperthyroidism were treated with cobaltous chloride by mouth. Clinical improvement was manifested by abatement of the tachycardia, reduction of basal metabolic rate, and rise in red blood cell count and blood hemoglobin content in four patients. These four patients also gave striking evidence of improvement in laboratory tests with radioiodine and three of them underwent thyroidectomy without complication after the cobalt therapy alone. The other four patients had less favorable results. One showed improvement in her preexisiting anemia but suffered recurrence (after temporary relief) of her symptoms of hyperthyroidism despite continued cobalt therapy; the other three did not respond to the cobalt at all as regarded their hypothyroidism, although one showed marked hematological improvement. The mode of action and indications for the use of cobalt in hyperthyroidism require further study.
strate consistent effects of cobalt (in doses up to 6 mg per kilogram per day) on thyroid I\(^{131}\) uptake, conversion ratios, and saliva radioactivity. More recently, however, Roche and Layrisse\(^3\) have shown that cobaltous chloride in doses of 150 mg.

### Table 2.—Treatment and Clinical Course

<table>
<thead>
<tr>
<th>Case</th>
<th>Cobaltous Chloride</th>
<th>No. of Days</th>
<th>Clinical Improvement</th>
<th>Plasma Radioactivity</th>
<th>Weight</th>
<th>Thyroidectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>130</td>
<td>35</td>
<td>++++</td>
<td>0</td>
<td>130</td>
<td>80</td>
</tr>
<tr>
<td>2</td>
<td>300</td>
<td>2</td>
<td>++++</td>
<td>0</td>
<td>143</td>
<td>88</td>
</tr>
<tr>
<td>3</td>
<td>300</td>
<td>2</td>
<td>++++</td>
<td>0</td>
<td>100</td>
<td>69</td>
</tr>
<tr>
<td>4</td>
<td>300</td>
<td>2</td>
<td>++++</td>
<td>0</td>
<td>100</td>
<td>80</td>
</tr>
<tr>
<td>5</td>
<td>150</td>
<td>2</td>
<td>++++</td>
<td>0</td>
<td>130</td>
<td>94</td>
</tr>
<tr>
<td>6</td>
<td>300</td>
<td>2</td>
<td>++</td>
<td>104</td>
<td>110</td>
<td>61</td>
</tr>
<tr>
<td>7</td>
<td>300</td>
<td>2</td>
<td>+</td>
<td>130</td>
<td>104</td>
<td>30</td>
</tr>
<tr>
<td>8</td>
<td>300</td>
<td>2</td>
<td>++</td>
<td>120</td>
<td>144</td>
<td>37</td>
</tr>
</tbody>
</table>

* Ambulatory treatment; BM at the end of treatment.

**This patient was ambulatory during the first 30 days of treatment and it was felt that he did not take his medication properly during this time.

per day in 12 nonanemic euthyroid adults led to a distinct fall in thyroid I\(^{131}\) uptake, in most cases after one week and in all cases after two weeks. In

![Fig. 1 (case 2).—Good response to cobalt therapy. Thyroidectomy.](image)

view of these findings, it was deemed worthwhile to try cobaltous chloride therapy as a means of controlling hyperthyroidism.

Eight cases of hyperthyroidism treated with cobaltous chloride are herein reported. In four of the cases there was marked clinical improvement, and in three of these a thyroidectomy was performed without complication after cobalt therapy alone (cases 1 and 2 have been briefly reported\(^2\)). In one case, there was initial response and later "escape," making it necessary to administer Lugol's solution before thyroidectomy; in the three remaining cases, there was no response to cobalt.

### Methods and Material

Thyroid uptakes were determined with a scintillation counter (Nuclear, model DS-1), saliva radioactivity,\(^4\) and conversion ratios\(^5\) with a well-type scintillation counter (Nuclear, model 3037 B) 24 hours after the administration of 50 \(\mu c\) of I\(^{131}\), correction being made if necessary for residual radioactivity. Cobalt was administered by mouth as cobaltous chloride in a 1% solution, in three divided doses after meals. The pulse was taken in the morning upon awakening.

![Fig. 2 (case 5).—Initial good response to cobalt therapy and later "escape." The administration of Lugol's solution in addition to cobalt led to rapid remission of the hyperthyroidism. Lugol's solution was continued after operation.](image)

All patients were hospitalized in the Hospital Vargas. The chief symptoms and signs are given in table 1 and the treatment indicated in table 2. Histological study was performed on all thyroid glands removed at operation.

### Results

The clinical course is summarized in table 2 and the chief laboratory findings before and at the end of treatment in table 3. Intolerance to medication in the form of epigastric pain, burning, and nausea was experienced by four patients, generally toward the start of treatment, while all other patients tolerated treatment well.

In one additional patient, treatment with cobalt could not be continued because of gastric intolerance to the drug. In the cases presented here, it was not necessary to discontinue medication entirely; in general, it was sufficient to stop cobalt for a day or two and resume therapy at a lower dosage.
level. After a week or two, the dosage could be raised again to its initial level without further trouble.

Comment

In five of the eight patients with hyperthyroidism treated with cobaltous chloride, there was clear-cut remission of symptoms and laboratory evidence of blocking of thyroid hormone synthesis.

Although it is well recognized that hyperthyroidism may subside spontaneously, it is unlikely that this should occur in five cases out of eight during a relatively short period of observation. In the early reports collected by Sattler, spontaneous remission is said to have occurred in from none to 50% of mild unoperated cases, with an average of 26%; recovery was described as usually occurring several years after onset. Since practically all patients today receive antithyroid treatment, there are no recent figures available on this point. Furthermore, we do not believe that a spontaneous remission would explain the laboratory evidence of block of thyroid hormone synthesis.

It was possible to perform thyroidectomy on three of the five patients who responded to cobalt without the addition of any other antithyroid medication. In one of the patients, who objected to operation (case 4), it was possible to continue cobalt therapy for 117 days without any untoward effect. After medication was discontinued, there was no return of symptoms; the patient died two months later of a cerebrovascular accident.

evidence of block in thyroid hormone synthesis, and a decrease in basal metabolic rate (BMR) to normal levels. Thyroidectomy was performed 45 days after the beginning of cobalt therapy.

In one patient (case 5) (fig. 2) there was clinical improvement at first and evidence of thyroid block. After 30 days of treatment, pulse and nervousness began again to increase and there was evidence of renewed thyroid activity; the goiter had increased markedly in size, and on the 70th day while cobalt therapy was being continued, Lugol's solution, 20 drops three times a day, was added, with resulting

The data on one of the patients who responded to cobalt (case 2) are presented in figure 1. In this case, the initial dose was 300 mg. of cobaltous chloride per day. This had to be stopped after three days because of nausea and epigastric distress. After 24 hours off treatment, cobalt therapy was resumed, at a dose of 150 mg. per day, without difficulty, so that after a week the initial dosage could again be started. There was definite clinical improvement after three weeks, associated with rapid and marked clinical improvement. Thyroidectomy was performed within 30 days of starting therapy with Lugol's solution. It is interesting that this patient had a nodular goiter, in which resistance to therapy is frequently observed.

Finally, in three cases, there was no response to therapy, even though cobalt was given in doses similar to those given in the previous four cases. The data on one such patient (case 7) are shown in figure 3. In spite of the administration of cobalt

![Fig. 3 (case 7).—No response to cobalt therapy. Good response to methimazole.](http://jama.jamanetwork.com/)

**Table 3.—Effect of Cobaltous Chloride on Laboratory Tests**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Response</th>
<th>A</th>
<th>B</th>
<th>A</th>
<th>B</th>
<th>A</th>
<th>B</th>
<th>A</th>
<th>B</th>
<th>A</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>15.3</td>
<td>15.0</td>
<td>4.2</td>
<td>4.7</td>
<td>+26</td>
<td>+1</td>
<td>78</td>
<td>17</td>
<td>76</td>
<td>5*</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>15.5</td>
<td>15.0</td>
<td>3.9</td>
<td>4.4</td>
<td>+22</td>
<td>-5</td>
<td>65</td>
<td>0</td>
<td>98</td>
<td>4*</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>15.8</td>
<td>17.7</td>
<td>4.4</td>
<td>5.1</td>
<td>+38</td>
<td>-6</td>
<td>51</td>
<td>17</td>
<td>92</td>
<td>6*</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>10.4</td>
<td>14.0</td>
<td>3.5</td>
<td>4.8</td>
<td>+44</td>
<td>+1</td>
<td>56</td>
<td>1</td>
<td>89</td>
<td>7*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Response and “escape”</th>
<th>A</th>
<th>B</th>
<th>A</th>
<th>B</th>
<th>A</th>
<th>B</th>
<th>A</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>5*</td>
<td></td>
<td>11.7</td>
<td>15.0</td>
<td>3.9</td>
<td>4.5</td>
<td>+42(+46)</td>
<td>74</td>
<td>61</td>
<td>91</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>12.1</td>
<td>14.3</td>
<td>4.5</td>
<td>4.5</td>
<td>+35</td>
<td>...</td>
<td>78</td>
<td>26</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>8.1</td>
<td>12.0</td>
<td>4.0</td>
<td>3.2</td>
<td>+31</td>
<td>...</td>
<td>55</td>
<td>40</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>9.1</td>
<td>9.1</td>
<td>3.3</td>
<td>3.0</td>
<td>+41(+21)</td>
<td>56</td>
<td>42</td>
<td>98</td>
</tr>
</tbody>
</table>

* A: before treatment; B: after treatment with cobalt.

\* This patient "escaped" treatment. The levels reached before escape were BMR, +15; thyroid uptake, 26; conversion ratio, 16; saliva radioactivity, 48.3.

**Blood Hemoglobin Level, (g./100 ml.)*

**Red Blood Cells, (Million/ml.)*

**BMR, %*

**24-Hr. [**131**I] Thyroid Uptake, %*

**Conversion Ratio, %*

**Saliva Radioactivity, 1,000 Counts/Min./30m.l.*
for 45 days, there was no change in clinical status, thyroid uptake, conversion ratio, BMR, or saliva radioactivity. Treatment with methimazole (Tapazole) resulted in rapid improvement, and thyroidectomy was performed after the addition of saturated potassium iodide solution. One of the three patients who did not respond to cobalt (case 6) had also a nodular goiter, and there was no response to drug therapy with methimazole or with potassium perchlorate. Hyperthyroidism was finally controlled in this case with 16 mc. of I\(^{131}\).

In all of the patients who responded to cobalt, blood hemoglobin levels and red blood cell counts rose under therapy (table 3). Of the three patients whose thyroid status did not change with cobalt, only one (case 7) showed a distinct rise in hemoglobin and red blood cell count, but this could not be attributed to cobalt, since this patient was given ferrous sulfate therapy simultaneously. The lack of response in the hematological indexes of two patients (cases 6 and 8) would suggest that, in these cases at least, cobalt was not properly absorbed and therefore did not reach in sufficient concentration either the thyroid gland or the bone marrow.

Histological study of the thyroid glands removed at operation (fig. 4) after cobalt treatment alone showed marked hyperplasia of follicular tissue with a high columnar, infolded epithelium. The sparse colloid contained abundant vacuoles. This appearance is not unlike that seen in patients treated with antithyroid drugs of the thiouracil type.

Cobalt appears to be clearly capable of blocking thyroid hormone synthesis in hyperfunctioning thyroid glands, as it does in normal thyroid,\(^{a}\) although its action is somewhat unpredictable, as witnessed by the three patients who showed no response whatever. The reason for this lack of response is at present unclear, as is in fact the mechanism of cobalt action on the thyroid. We feel, however, that, in view of the good results obtained in several of the cases, it might be interesting to submit this drug to further therapeutic trial in hyperthyroidism.

Summary

Eight patients with hyperthyroidism were treated with varying doses of cobaltous chloride by mouth. In four of these, there was marked clinical improvement and evidence of block of thyroid hormone synthesis. In three of these cases a thyroidectomy was performed; the histological appearance was that of follicular hyperplasia. One of the four patients who responded was carried for 117 days on cobalt therapy, with apparent clinical remission. One patient who responded initially later "escaped" the effect of the drug and had to be given Lugol's solution before operation. In three cases, there was no response to the drug; one of these patients did not respond to methimazole or potassium perchlorate, and had to be given I\(^{131}\) therapy.

Apartado 1827 (Dr. Roche).

References


