Clinical Observations on Thyreoidismus Medicamentosus Due to
Weight Reducing Pills in Japan

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Synopsis

Over a hundred cases of toxicosis due to weight reducing drugs containing thyroid
preparations were recently observed in various areas in Japan. The most frequent cause
was the drug “Baset Super” which contains 20 mg of Jodocasein and 20 mg of desiccated
thyroid per tablet. Cases of toxicosis due to weight reducers containing Jodocasein have
not previously been reported. The patients had generally been taking 10 to 20 tablets per
day for over 6 months. In these cases, the chief complaints of the patients were palpitation,
emaciation, diarrhea, amenorrhea and psychic abnormalities. A few patients seemed to
have an addiction for the thyroid containing drug. In some cases, suppressed state of
thyroid and amenorrhea were observed long after discontinuation of the drug.

There are only few reports of scattered
cases of thyrotoxicosis due to weight reducing
drugs containing thyroid preparation through-
out the world and there have been few experi-
mental studies on this condition. This paper
summarizes the findings on more than one
hundred cases observed recently in Japan and
detailed observations on illustrative cases. We
examined eighteen patients who were admitted
to Tokushima University Hospital and made
follow up studies on them for several years
after their discharge from hospital. Records
of 105 other cases were collected in coopera-
tion with medical and psychiatrical clinics of
medical school and public hospitals through-
out Japan. These records included the
patients who had thyrotoxic symptoms but
without apparent goiter and had self-medica-
tion of thyroid drugs recognized. Data on the
latter cases were chiefly analyzed according
to age of incidence, geographical distribution
and sort of thyroid preparations.

Illustrative Cases

The case reported here illustrates the typical
course of thyroid intoxication.

Case 1: The patient, N. M., a 22 year old
housewife was admitted to the 1st. Clinic of
Internal Medicine of Tokushima University
Hospital in 1963, complaining of palpitation,
diarrhea and emaciation. Her anamnesis was
as follows. She was healthy and weighed 54
kg before she developed palpitation at the age
of 19. She married when she was 20 and her
husband noticed that she was losing con-
siderable weight. As palpitation, vomiting
and emaciation increased she was admitted
to a public hospital. Her BMR was 160% above normal although she had no goiter.
She was treated with antithyroid drug and
discharged with some clinical improvement.
However in 1965, she suffered from fluttering
sensation and severe prostration and she was
admitted to our clinic.

Physical examination on admission. The
patient was emaciated. She was 153 cm tall
and weighed 28.5 kg. Finger tremor was severe and her behavior was unstable. She had no exophthalmus and her thyroid was normal. Her pulse was regular and its rate was 100 to 120 per minute. Physical examination of her chest and abdomen showed no abnormalities. She had diarrhea with four to six watery bowel movements a day and no menstruation.

Laboratory data. Her chest X-ray was normal and her ECG showed sinus tachycardia. Hb 77%, RBC 451 x 10⁴, WBC 5,800, BMR + 104%, Serum PBI 16.8 μ/dl, 24 hour-thyroidal ¹³¹I-uptake 0.4%, ¹³¹I-PBI conversion ratio 7%. Thyroid scintigram showed absence of activity throughout. Blood cholesterol 105 mg/dl.

Course in hospital: From these findings we thought that she might have been taking some thyroid preparation such as weight reducing pills. We questioned her frequently about this but she would not admit that she had taken any and we could not find any pills in her possession. After one month she became more prostrated and restless and her behavior became erratic and somewhat lethargic. She continued to have nausea, vomitting and diarrhea and she became unable to walk. Her serum potassium level was 3.0 mEq/l. While she was in this state we found some tablets containing a thyroid preparation behind her in her bed. Accordingly we kept her in isolation. After 1 week, her palpitation, nervousness and diarrhea gradually decreased. Her BMR dropped to normal after 1 month, gradually decreased to the subnormal level of -15% after 3 month and then increased to -10 to -5%, remaining at this level for a long time. At the time of her discharge she confessed that she had been taking the weight reducer named Baset Super (one tablet of this drug contains 20 mg of desiccated thyroid and 20 mg of Jodocasein). She bought it at a chemist and had been taking 10 to 20 tablets a day for 3 years. One and half years after she stopped taking this drug we examined her thyroid function with the following results:

BMR -5%, PBI 5.6 μ/dl, Triosorb (T₃-resin sponge uptake) 26%, 24 hour-thyroidal ¹³¹I-uptake 11%. Thyroid scintigram, poorly visualized. TSH-test normal. She still suffered from amenorrhea and weighed only 31 kg and she complained that she readily became fatigued and felt cold. After 5 years, she still had amenorrhea and was thin.

This case was considered as a typical case of severe thyroid intoxication and the clinical picture can be summarized as follows. During medication hypermetabolism appears without goiter and after cessation of the thyroid drug, suppressed thyroidal activity was observed for over a year.

The next case illustrates the psychic manifestation of toxicosis.

Case 2: The patient, Y. K., a 20 year old woman was admitted to Tokushima University Hospital in 1964 complaining of psychic disturbances. Her anamnesis was as follows. She had taken a drug containing a thyroid preparation habitually since she was 18 years of age at college. She became restless and unable to study and left college. Inability to concentrate and sluggishness of thought gradually developed. When she returned to her home, her parents noticed her psychic abnormalities and found that she was taking the drug. Her family kept her in confinement but she could not abstain from the drug and so she was forcibly admitted to a psychiatrical clinic with the symptom of irritability. After 1 month she became well and was discharged. Soon after her discharge she started to take the drug again and visited us.

Course in the hospital: She was thin and restless with no finger tremor or palpable thyroid. Her pulse rate was normal. BMR +38%, Triosorb test 52%, 24 hour-thyroidal ¹³¹I-uptake 3%. She was excited and depressed and showed emotional instability but no hallucinations. One month after cessation of the drug she became calm and was discharged. However, she soon started to take the drug again and committed suicide with hypnotics. This case was particular in that she abused
thyroid drug frequently and seemed to be addicted to it.

**Clinical Observations**

Clinical observations on 18 cases are summarized as follows.

**Symptoms:** The patients visited the physicians complaining of palpitation, emaciation, psychic irritability, menstrual abnormalities, diarrhea and loss of hair. Loss of weight was especially prominent and some cases had become half their usual weight. Transient psychic abnormalities were observed in 33% of the patients. These included restlessness, nervousness, agitation and depression. One case suffered from pseudohallucinations. Two cases were acutally admitted to mental institutions with suspected psychosis but they all recovered from psychological abnormalities after cessation of the thyroid drugs.

Several patients first visited their doctors complaining of oedema of the face, fatigueability, obstipation, coldness of the extremities and amenorrhea. The main details of these cases are given in Table I. In a few patients of these cases we had the impression that physical examination and laboratory tests seemed to show masked hypothyroidism. Detailed histories suggested that these cases had been taking excessive thyroid drugs for prolonged periods and it seemed to be the withdrawal symptom.

**Laboratory findings:** In the patients under thyroid medication the characteristic findings on examination were abnormal thyroid function tests. The ranges of data were as follows: BMR, +50% to +100%, Blood PBI 8 ~ 20 γ/dl, Trisosorb test 40 to 60%. Contrary to the high value in the above tests, 24-hour-thyroidal 131I-uptake was low ranging from 0 to 10%. The 131I-PBI conversion ratio was also very low. The thyroid scintigram was usually well not visualized. The TSH-test was normal. This discrepancy among the thyroid tests was the most characteristic finding in these cases, and indicated that, they had an abnormally high peripheral level of thyroid hormone but abnormally low thyroid function. This led us to suspect that they suffered from exogenic thyroid hormonosis, namely thyrotoxicosis factitia.

**Other laboratory data:** Serum alkaline phosphatase was high (10.5 ~ 14.3 Bodansky U.) during thyroid medication and decreased with time after discontinuation of the drug.

<table>
<thead>
<tr>
<th>Case</th>
<th>Symptoms</th>
<th>Daily dose of thyroid taking</th>
<th>Situation of medication on admission</th>
<th>Thyroid function tests</th>
<th>scintigram</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. A. K. (24,f)</td>
<td>oedema on face and leg, emaciation, amenorrhea</td>
<td>Buset Super 10 Tab. or more, 1.5 yr.</td>
<td>1.5 yr. after cessation of thyroid</td>
<td>BMR -11, PBI 7.0, T3-Test 22, 24hr-131I-uptake 27</td>
<td>slightly diminished uptake</td>
</tr>
<tr>
<td>2. A.N. (19,f)</td>
<td>oedema on face, depression, lassitude</td>
<td>B.S. 10 Tab. or more, 1.5 yr.</td>
<td>6 month after cessation of thyroid</td>
<td>BMR -19, PBI 4.9, T3-Test 30, 24hr-131I-uptake 8</td>
<td>poorly visualized</td>
</tr>
<tr>
<td>3. M.M. (20,f)</td>
<td>loss of hair, lassitude</td>
<td>B.S. 6 ~ 9 Tab.</td>
<td>2 yr. after cessation of thyroid</td>
<td>BMR -14, PBI 5.0, T3-Test 29, 24hr-131I-uptake 13</td>
<td>poorly visualized</td>
</tr>
<tr>
<td>4. S.T. (22,f)</td>
<td>lassitude, amenorrhea numbness of leg</td>
<td>B.S. 10 Tab.</td>
<td>2 yr. after cessation of thyroid</td>
<td>BMR -17, PBI 30, T3-Test 27</td>
<td>normally visualized</td>
</tr>
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</table>
The BSP-test showed slight retention (12.5 ~ 20%) in some cases. Serum potassium was rather low in cases with diarrhea and in one case was 3.0 mEq/l during intoxication. The ECG of this case had depressed ST, T segments respectively. Urinary adrenal steroid excretion and Thorn's test were normal.

**Treatment and details of follow up studies:**
The patients had to be hospitalized and kept in isolation to prevent them from continuing to take the thyroid drug. Superintendence was necessary to ensure this. Medical treatment was necessary in cases with dehydration and hypopotassemia due to diarrhea and sometimes sedatives were required in cases with nervous irritability. Somatic abstinence signs were not observed on abrupt discontinuation of the drug. The general course after discontinuation of the drug was as follows. The BMR decreased gradually, reached normal after about 1 to 3 months and decreased below normal to -15%. Then it gradually increased to normal or a slightly subnormal level after 6 months or more. In a few cases, amenorrhea and emaciation also persisted for a long time. These sequelae were usually found in cases who had taken more than 10 tablets of Baset Super daily for over 1 year. The prognoses of the 18 cases who were followed up for over 6 months after their discharge were as follows: 9 cases were completely cured; 5 cases started taking the drug again (abuse or thyroid dependence suspected); depressed thyroid activity continued in 4 cases; 4 cases suffered prolonged emaciation; amenorrhea persisted in 3 cases; 1 case committed suicide.

**Survey on the Records**

Statistical analysis on 105 records and our cases was made of its situation of occurrence. The cases were observed from 1965 to 1969 with maximum frequency in 1967. These cases probably represents only part of the total cases in Japan because the survey was limited. They included cases from all prefectures in Japan. They were all female and varied in age from 15 to 55 years old, and cases in their twenties being the most common. Many of these patients had taken a thyroid preparation for 6 months to 2 years and one had taken it for 7 years. Of thyroid preparations, Baset Super was most commonly used and 20 per cent of the cases had taken the tablets of desiccated thyroid only.

**Discussion**

Weight reducers containing thyroid extracts have widely been used throughout the world and there are reports of isolated cases of toxicity. In the United States of America sale of these drugs is now illegal under the Federal law. However, no previous cases of this type have been reported in Japan. The clinical status of this condition has been termed thyrotoxicosis factitia but we know of no cases of toxicosis due to weight reducers containing Jodocasein.

Jodocasein was investigated by Reineke (1946) and others. Clinically, it has occasionally been used in treatment of cases of hypothyroidism in Japan. In physiological tests using tadpoles, Minato and Tanaka (1950) demonstrated that the physiological effects of Jodocasein was more active than desiccated thyroid. And we also noticed in animal experiments that Jodocasein was equally effective on weight reduction with desiccated thyroid (Miyoshi and Ohno, 1966). So the hormonal activity of 1 tablet of Baset Super was presumed equivalent to more than 40 mg of desiccated thyroid. Many patients took 10 to 20 tablets of Baset Super a day, which are equivalent to about 0.4 to 0.8 g or more of desiccated thyroid. This is 2 to 3 times as much as the prescribed dose and the patients were easily in a toxic state. The clinical condition of suppressed thyroidal activity and other sequelae observed in the presented cases long after discontinuation of thyroid drugs seemed to continue longer than
The term thyrotoxicosis factitia refers to the thyrotoxic state only, so we proposed the term “Thyreoidismus Medicamentosus” for the whole course of this condition of thyroid intoxication, including the toxic state, suppressed thyroid state, psychic abnormalities and other sequelae. We may summarize the whole course as follows (Fig. 1).

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References


