A Clinical Case of Hypoglycemia Suggestive of Early Diabetes Mellitus

Kiyohiko Yoshikawa

Department of Internal Medicine (Dr. Y. Hatakeyama),
Iwaki Kyoritsu Hospital, Uchigo

A clinical case of hypoglycemia was reported. Hypoglycemia in this case was characterized by delayed recovery and low stationary values of blood sugar in insulin and tolbutamide tests. Since the results of glucose tolerance test in this case met precisely the diagnostic criteria of early diabetes described by Seltzer et al., a possible relation between hypoglycemia and early diabetes was discussed on the basis of laboratory examinations. The follow-up study of the case is still continued.

In 1956 Seltzer et al. published a report on the clinical pictures of early diabetes mellitus with hypoglycemic symptoms. Their report offered a very interesting and important endocrinological problem in early diabetes in connection with the concept of prediabetic state. While I was interested in the above subject, a clinical case exhibiting precisely the same result of the glucose tolerance test (G.T.T.) as that reported by Seltzer et al. was admitted to our hospital. The observation was continued for three and a half years on this case which was in the condition designated by Seltzer et al. as an early manifestation of diabetes mellitus. The present paper deals with the results obtained.

REPORT OF CASE

A 31-year-old male, M.M., without occupation was admitted to our hospital with the main complaints of paroxysmal palpitation in hunger and a sensation of strangulation on the left anterior part of the chest. There was no family history of diabetes and giant babies. Nothing particular was mentioned in his past history. He had been born normally at full term.

The history of the present illness dated from the midnight in the end of July, 1962, when the patient had a sudden and severe palpitation after rising from the bed for stool and felt as if he had fallen into swoon. He visited a hospital immediately and was told that he had a high systolic blood pressure around 170 mm Hg. He was admitted to the hospital as having hypertension. In the course

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of the subsequent days, the above-mentioned symptoms often developed in
hunger. He left the hospital without improvement and consulted other physicians.
Hypertension was diagnosed by all of them. From early October of the same
year he had often a sensation of strangulation on the left anterior part of the
chest. Because the systolic blood pressure exceeded 200 mm Hg, he was treated
by a practitioner under the diagnosis of hypertension with suspected myocardial
infarction. His conditions, however, became only worse. From early January
1963, his vision was blurred and he felt dryness of the mouth. He was then
admitted to the ward of internal medicine of our hospital on the 12th March
of the same year.

Physical examinations at admission

The patient was of normal build and was in a normal nutritional condition.
The skin and visible mucous membrane exhibited neither anemia nor icterus. No
abnormality was observed on the head and face. The pupils were circular, and the
light reflex was normal. The tongue had a slight fur but was moist. No systemic
swelling of lymph nodes was present. The pulse was irregular but of good
tension. At auscultation and percussion, the limit of cardiac dullness was
enlarged by one finger's breadth to the left. The heart sound was pure.
Pulmonary auscultation revealed nothing abnormal. The abdomen was flat
without any palpable tumor and without pain or resistance on pressure. The
liver, spleen, and kidneys were not palpable. The legs were not edematous, and
the tendon reflex was normal without any pathologic reflexes. The blood
pressure was 160/108 mm Hg. His height was 155 cm and weight, 54 kg.

Laboratory examinations

Urinalysis. The urinary volume was practically normal. The urine was
positive for sugar.

Blood picture. There was nothing abnormal in erythrocytes and hemoglobin,
but leukocytosis (leukocyte count: 14,900) and neutrophilia (neutrophils : 73%)
were observed.

Blood and serum examinations. Liver function tests were normal and there
was no hypercholesterolemia. Electrolytes, serum protein fractions, and NPN
were all within the normal range.

The endocrine system. The basal metabolic rate was normal. The sella
turcica was of a normal size on the radiogram. Urinary 17-KS and 17-OHCS were
both within the normal range.

E.C.G. Ventricular premature beats were noted.

Other examinations. The serum pyruvic acid value was normal. The
chest x-ray picture exhibited no particular abnormality. The fundal ex-
aminations revealed neither retinopathy nor other pathological findings. X-ray
examinations of the gastrointestinal tract revealed the presence of a mild degree
Fig. 1. Variations in blood sugar curve in oral glucose tolerance test with 50g of glucose. 1: March 14, 1963. 2: June 6, 1963. 3: January 10, 1964. 4: April 14, 1964.

Hypoglycemia and Early Diabetes Mellitus

Behavior of blood sugar (cf. Fig. 1). The fasting blood sugar level as determined by the Fujita-Iwatake method was 90.4 ml/100 ml. Oral glucose tolerance test was performed with 50 g of glucose: the values at 1 hour and 2 hours were 191.4 mg/100 ml and 151.4 mg/100 ml, respectively, thus exhibiting a diabetic curve. But, the value at 3 hours after the administration showed a peculiar decline to only 45.2 mg/100 ml.

Course after admission

The G.T.T. levels following admission are presented in Fig. 1. The levels thus showed fairly distinctive variations. Soon after his admission, the patient was given 300 g of carbohydrate together with the administration of Amisalin (procaine amide) and Balance (chlordiazepoxide) tablets simultaneously. The G.T.T. on June 6, 1963, showed a fasting blood sugar of 102.6 mg/100 ml and, 1 hour after the glucose loading, 182.7 mg/100 ml. At 2 hours, the level showed an unusually marked decline, i.e., down to 55.6 mg/100 ml. Since September 1963, the hypoglycemic condition was intensified. The G.T.T. on September 11 yielded the following values: fasting blood sugar, 73.0 mg/100 ml; at 1 hour, 146.1 mg/100 ml; at 2 hours, 62.6 mg/100 ml; and at 3 hours, 62.6 mg/100 ml. The results of G.T.T. performed on December 12, 1963, were: fasting blood sugar, 109.6 mg/100 ml; at 1 hour, 161.8 mg/100 ml; at 2 hours, 76.5 mg/100 ml; and at 3 hours, 78.3 mg/100 ml. The maximum glucose level in the hyperglycemic phase was thus found lowered. Following the prescription of a carbohydrate rich diet (carbohydrate 500 g) since December 11, 1963, no rise
in the blood sugar level was observed at first. At the same time, incidence of hypoglycemic symptoms in hunger became frequent. The patient was, therefore, returned to the carbohydrate-restricted diet from January 30, 1964 (carbohydrate, 300 g). A tranquilizer was given, too. The G.T.T. on April 14, 1964, gave the values presented in Fig. 1. The fasting blood sugar was 90.0 mg/100 ml; the blood sugar level at 1 hour was 167.0 mg/100 ml; at 2 hours 99.1 mg/100 ml; and at 3 hours 57.4 mg/100 ml. Subjective symptoms of the patient were improved.

In order to see the relationship between the prediabetic state and hypoglycemia as described by Seltzer et al., the intravenous sodium tolbutamide test was carried out, and insulin blood sugar reaction in a group of mild diabetics including the present patient. They were divided into a non-treated diabetic group, a treated diabetic group and a group of hypoglycemic patients (Tables 1, 2, 3, and 4).

We have already pointed out, that the pattern of blood sugar curves in patients with slight diabetes or hypoglycemia are generally determined by the following four factors: fasting blood sugar level, index or speed of blood sugar decline, index or speed of blood sugar recovery and stationary blood sugar value. The effects of the four factors are diagrammatically demonstrated in Fig. 2. The reaction of blood sugar to insulin was determined with the method described by Saito. The intravenous sodium tolbutamide test was performed in the following manner. After intravenous injection of the sodium tolbutamide, blood was drawn every 10 minutes up to 3 hours after the injection.

Fig. 2. Intravenous sodium tolbutamide and insulin blood sugar reaction (schematic blood sugar curve).

A : Fasting blood sugar level. A-m/T: Index for blood sugar decline.
m : Minimal blood sugar level. M-m/t: Recovery index.
M : Maximal blood sugar level. A-m/A: Time for maximal decline.
T : Time for decline. A-m/A/T: Sensitivity index.
t : Time for recovery. M-m<10 mg/100 ml: No recovery effect.
c : Stationary value.
Fig. 3. Blood sugar levels following sodium tolbutamide and insulin injection.
- Subcutaneous injection of insulin (5 u)
- Intravenous injection of sodium tolbutamide (1 g)

Fig. 4. Blood sugar levels following 50 g GTT, 100 g GTT and PGTT.
- June 29, 1964 GTT (Glucose 20 ml of 50%, i.v. inj.)
- April 14, 1964 GTT (Glucose 50 g per os)
- June 25, 1964 PGTT (Prednisolone 10 mg per os; then glucose 50 g per os)
- June 22, 1964 GTT (Glucose 100 g per os)
and thereafter every 30 minutes up to 5 hours. The blood samples so obtained were determined for sugar contents. When the minimum and maximum blood sugar levels were thus determined, the length of time from the tolbutamide injection to the minimum blood sugar value and that from the minimum value to the maximum value in the recovery phase were defined as the decline and recovery times, respectively.

Variation in blood sugar levels following the intravenous injection of sodium tolbutamide are presented in Tables 1 and 2. Observations were made on four groups of subjects, normal, liver-damaged, hypoglycemic, and mild diabetic. The average values in the normal group were: fasting blood sugar, 97.8 mg/100 ml; index of blood sugar decline, 0.99; blood sugar recovery index, 1.29; and stationary value, 97.9 mg/100 ml. Those for the liver-damaged group were as follows: fasting blood sugar, 109.0 mg/100 ml; index of blood sugar decline, 0.86; blood sugar recovery index, 0.95; and stationary value, 91.8 mg/100 ml. As compared with the normal group, this group thus exhibited lower indices of blood sugar decline and recovery.

The average values in the hypoglycemic group were: fasting blood sugar, 86.6 mg/100 ml; index of blood sugar decline, 0.93; blood sugar recovery index, 0.49; and stationary value, 58.8 mg/100 ml. The fasting blood sugar level and the index of blood sugar decline were thus not much different from those in the normal group, but the recovery index was much lower and the stationary value indicated hypoglycemia, being definitely different from the value in the

![Blood sugar levels](image)

**Fig. 5.** Intravenous sodium tolbutamide test (1 g).

--- May 30, 1964
--- June 27, 1964
<table>
<thead>
<tr>
<th>Blood sugar decline rate (%)</th>
<th>20 min</th>
<th>30 min</th>
<th>60 min</th>
<th>90 min</th>
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<tr>
<td>Hypoglycemia time (minute)</td>
<td>6.3</td>
<td>4.7</td>
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<td>Glucose tolerance index</td>
<td>82.3</td>
<td>4.6</td>
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<td>0.12</td>
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<td>Sensitivity index (%)</td>
<td>67.7</td>
<td>29.2</td>
<td>0.73</td>
<td>0.73</td>
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<tr>
<td>Rate of maximum recovery</td>
<td>81.1</td>
<td>5.0</td>
<td>0.19</td>
<td>0.19</td>
</tr>
<tr>
<td>Blood sugar index of blood</td>
<td>81.1</td>
<td>5.0</td>
<td>0.19</td>
<td>0.19</td>
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<tr>
<td>Index of blood flow after</td>
<td>81.1</td>
<td>5.0</td>
<td>0.19</td>
<td>0.19</td>
</tr>
<tr>
<td>decline</td>
<td>81.1</td>
<td>5.0</td>
<td>0.19</td>
<td>0.19</td>
</tr>
<tr>
<td>Time for recovery (minute)</td>
<td>16.9</td>
<td>0.43</td>
<td>0.43</td>
<td>0.43</td>
</tr>
<tr>
<td>Maximum blood sugar (mg/dl)</td>
<td>77.0</td>
<td>0.97</td>
<td>0.97</td>
<td>0.97</td>
</tr>
<tr>
<td>Minimum blood sugar (mg/dl)</td>
<td>77.0</td>
<td>0.97</td>
<td>0.97</td>
<td>0.97</td>
</tr>
</tbody>
</table>

**Table 1. Results of intravenous sodium tolbutamide test in mild diabetics**

Hypoglycemia and Early Diabetes Mellitus 323

**Non-treated group**

- B.Y.: 88.5
- Y.S.: 87.2
- M.S.: 78.0
- Y.M.: 102.6
- T.S.: 129.0

**Treated group**

- A.S.: 142.6
- Y.O.: 133.1
- T.A.: 153.9

(Average) Y.S. = 87.2
(Average) M.S. = 78.0
(Average) Y.M. = 102.6
(Average) T.S. = 129.0

5 cases

(Average) T.A. = 153.9
(Average) Y.O. = 133.1
(Average) A.S. = 142.6

3 cases
TABLE 2. Results of intravenous sodium tolbutamide test in normal, normal group.

The values in mild diabetics divided into non-treated and treated groups averaged as follows, respectively: blood sugar level, 10.4.1 mg/100 ml; the index of blood sugar decline, 0.36 and 0.44; the recovery index, 0.17 and 0.15; and the stationary value, 77.0 mg/100 ml and 96.1 mg/100 ml. The fasting blood sugar level and the stationary value were not much different from those in the normal group, but the index of blood sugar decline and the recovery index were evidently different from those in the normal group.

Comparing the results of the intravenous sodium tolbutamide test between the group of mild diabetics and the group of hypoglycemic patients, there was not much difference in fasting blood sugar. While the group of diabetics exhibited low indices of blood sugar decline and recovery, the group of hypoglycemic patients showed normal index of blood sugar decline but extremely low recovery index. It was noteworthy that the group of hypoglycemic patients exhibited distinctly lowered stationary values.

The results of comparative determinations of the insulin blood sugar reaction of the three groups, i.e., normal, hypoglycemic and diabetic, are presented in Tables 3 and 4. In the normal group, the index of blood sugar decline was 22.0, the recovery index 15.8, and the stationary value 90.7 mg/100 ml. In the hypoglycemic group, there was no recovery effect observed in any of the cases. The stationary value was 56.6 mg/100 ml, a markedly lower level than in the normal group. In the non-treated and treated groups of mild diabetics, the index

<table>
<thead>
<tr>
<th>Kinds of groups</th>
<th>Fasting blood sugar (mg/100ml)</th>
<th>Minimum blood sugar (mg/100ml)</th>
<th>Maximum blood sugar (mg/100ml)</th>
<th>Time for decline (minutes)</th>
<th>Time for recovery (minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal group</td>
<td>97.8</td>
<td>63.1</td>
<td>90.6</td>
<td>30</td>
<td>19.3</td>
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<tr>
<td>Liver damaged group</td>
<td>109.0</td>
<td>78.4</td>
<td>108.0</td>
<td>43.3</td>
<td>40</td>
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<tr>
<td>Hypoglycemic group</td>
<td>86.6</td>
<td>43.5</td>
<td>67.0</td>
<td>46.1</td>
<td>52.2</td>
</tr>
<tr>
<td>Diabetic group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-treated group</td>
<td>104.1</td>
<td>76.5</td>
<td>90.5</td>
<td>36.6</td>
<td>93</td>
</tr>
<tr>
<td>Treated group</td>
<td>121.6</td>
<td>93.6</td>
<td>104.4</td>
<td>50</td>
<td>95</td>
</tr>
</tbody>
</table>
Hypoglycemia and Early Diabetes Mellitus

It may be summarized from the above-mentioned results of the intravenous sodium tolbutamide test and the insulin blood sugar reaction that there was no particular difference between the mild diabetic and hypoglycemic groups in terms of the fasting blood sugar, but that there was a marked difference in the stationary value. This finding is worthy of special attention.

Immunoassay of insulin was performed with two antibody systems by the Morgan and Lazarow method. Blood specimens were collected from this patient in the fasting and in 1/2 hour, 1 hour, 2 hours, and 3 hours after ingestion of 50 g of glucose. Insulin values were: 20 ìU/ml, 32 ìU/ml, 72 ìU/ml, 46 ìU/ml, and 26 ìU/ml, respectively. The maximal insulin value was within the normal range, but the appearance of the peak was delayed.

At the same time, the blood 17-OHCS level was measured. The values corresponding to the above-mentioned time scale were 18 ìg/ml, 17 ìg/ml, 18 ìg/ml, 16 ìg/ml, and 14 ìg/ml, respectively. Three hours’ value of 17-OHCS against that of insulin was lower than in normal controls. The result may account in part for the lowered capacity of blood sugar restoration.

The patient has been kept under clinical observations up to the date of the publication of this report. Manifest signs of diabetes have not yet developed. The follow-up study is still continued.

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Hepatocellular dysfunction, hypoglycemic, and mild diabetic groups (average values)

<table>
<thead>
<tr>
<th>Index of blood sugar decline</th>
<th>Blood sugar recovery index</th>
<th>Rate of maximum decline (%)</th>
<th>Sensitivity index</th>
<th>Stationary value (mg/100ml)</th>
<th>Blood sugar decline rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.99</td>
<td>1.29</td>
<td>30.1</td>
<td>0.99</td>
<td>97.9</td>
<td>30  36  14</td>
</tr>
<tr>
<td>0.86</td>
<td>0.95</td>
<td>28.1</td>
<td>0.75</td>
<td>91.8</td>
<td>22.7 29.3 14.6</td>
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<tr>
<td>0.93</td>
<td>0.49</td>
<td>47.2</td>
<td>1.04</td>
<td>58.8</td>
<td>33.1 36.0 50.3</td>
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<tr>
<td>0.36</td>
<td>0.17</td>
<td>16.9</td>
<td>0.43</td>
<td>77.0</td>
<td>0.88 11.1 21.6</td>
</tr>
<tr>
<td>0.44</td>
<td>0.15</td>
<td>18.3</td>
<td>0.42</td>
<td>96.1</td>
<td>3.5  6.8 11.8</td>
</tr>
</tbody>
</table>

of blood sugar decline was 19.1 and 21.1, the recovery index 14.0 and 24.0; and the stationary value, 74.0 mg/100 ml and 81.7 mg/100 ml, respectively, thus exhibiting no marked difference from the values of the normal group.
### Table 3. Insulin blood sugar reaction in mild diabetics

<table>
<thead>
<tr>
<th></th>
<th>Fasting blood sugar (mg/100ml)</th>
<th>Minimum blood sugar (mg/100ml)</th>
<th>Maximum blood sugar (mg/100ml)</th>
<th>Time for decline (hours)</th>
<th>Time for recovery (hours)</th>
<th>Index of blood sugar decline</th>
<th>Blood sugar recovery index (%)</th>
<th>Rate of maximum decline (%)</th>
<th>Sensitivity index (mg/100ml)</th>
<th>Stationary value (%)</th>
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<tr>
<td>Non-treated group (5 cases)</td>
<td>103.0</td>
<td>67.4</td>
<td>(No recovery effect)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>K.N.</td>
<td>87.0</td>
<td>62.0</td>
<td>65.6</td>
<td>2</td>
<td>0.5</td>
<td>12.4</td>
<td>6.6</td>
<td>28.5</td>
<td>14.3</td>
<td>67.7</td>
</tr>
<tr>
<td>T.S.</td>
<td>120.0</td>
<td>72.6</td>
<td>110.8</td>
<td>1.5</td>
<td>3.1</td>
<td>31.6</td>
<td>18.8</td>
<td>39.5</td>
<td>26.2</td>
<td></td>
</tr>
<tr>
<td>M.S.</td>
<td>107.8</td>
<td>67.4</td>
<td>83.1</td>
<td>3</td>
<td>1.5</td>
<td>13.4</td>
<td>16.8</td>
<td>37.5</td>
<td>12.5</td>
<td>80.4</td>
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<tr>
<td>Y.M.</td>
<td>97.4</td>
<td>67.4</td>
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<td></td>
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</tr>
<tr>
<td>(Average)</td>
<td>103.0</td>
<td>67.4</td>
<td>86.5</td>
<td>2.1</td>
<td>1.8</td>
<td>19.1</td>
<td>14.0</td>
<td>35.1</td>
<td>17.6</td>
<td>74.0</td>
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<tr>
<td>Treated group (3 cases)</td>
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<td>68.7</td>
<td>86.6</td>
<td>2.8</td>
<td>2.3</td>
<td>21.1</td>
<td>24.0</td>
<td>44.6</td>
<td>20.1</td>
<td>81.6</td>
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<td>T.A.</td>
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<tr>
<td>Y.O.</td>
<td>153.1</td>
<td>63.1</td>
<td>97.0</td>
<td>2.5</td>
<td>2.5</td>
<td>36.0</td>
<td>39.6</td>
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<td>(Average)</td>
<td>124.7</td>
<td>68.7</td>
<td>86.6</td>
<td>2.8</td>
<td>2.3</td>
<td>21.1</td>
<td>24.0</td>
<td>44.6</td>
<td>20.1</td>
<td>81.6</td>
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</table>

### Table 4. Insulin blood sugar reaction in normal, hypoglycemic, and diabetic groups

<table>
<thead>
<tr>
<th></th>
<th>Fasting blood sugar (mg/100ml)</th>
<th>Minimum blood sugar (mg/100ml)</th>
<th>Maximum blood sugar (mg/100ml)</th>
<th>Time for decline (hours)</th>
<th>Time for recovery (hours)</th>
<th>Index of blood sugar decline</th>
<th>Blood sugar recovery index (%)</th>
<th>Rate of maximum decline (%)</th>
<th>Sensitivity index (mg/100ml)</th>
<th>Stationary value (%)</th>
</tr>
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<tbody>
<tr>
<td>Normal group (7 cases)</td>
<td>101.7</td>
<td>83</td>
<td>95</td>
<td>1.5</td>
<td>1.5</td>
<td>22.0</td>
<td>15.8</td>
<td>12.0</td>
<td>19.1</td>
<td>90.7</td>
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<tr>
<td>Hypoglycemic group (8 cases)</td>
<td>81.2</td>
<td>54.2</td>
<td>60.6</td>
<td>(No recovery effect)</td>
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<td>10.5</td>
<td>56.6</td>
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<td>Non-treated group (4 cases) (Average)</td>
<td>103.0</td>
<td>67.4</td>
<td>86.5</td>
<td>2.1</td>
<td>1.8</td>
<td>19.1</td>
<td>14.0</td>
<td>35.1</td>
<td>17.6</td>
<td>74.0</td>
</tr>
<tr>
<td>Treated group (5 cases) (Average)</td>
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<td>2.3</td>
<td>21.1</td>
<td>24.0</td>
<td>44.6</td>
<td>20.1</td>
<td>81.6</td>
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</table>
Hypoglycemia and Early Diabetes Mellitus

**DISCUSSION**

As diagnostic criteria for early diabetes, Seltzer et al.\(^1\) have specified the symptoms in Table 5. Frequent occurrence of periodically developing hypoglycemic symptoms is referred to as one of the important signs in early diabetes. Another characteristic of early diabetes is hypoglycemic symptoms occurring from 3 to 5 hours after meals. The G.T.T. value by the Somogyi-Nelson venous blood method is not less than 160 mg/100 ml at one hour and not less than 120 mg/100 ml at 2 hours but with subsequent decline to 50 mg/100 ml or lower. A third prominent feature in early diabetes is a family history or heredity of diabetes, obesity, and frequent occurrence of giant babies. The outcome of the G.T.T. characterizing early diabetes is demonstrated in the following pattern. The initial hyperglycemic phase is associated with lowered rate of insulin secretion. The hypoglycemic phase is brought about by delayed secretion of insulin. Although the insulin capacity of Langerhans' islet is normal, excessive insulin secretion is regarded to take place in the hypoglycemic phase and to lead to precipitous fall of blood sugar levels.

The G.T.T. findings in our case were exactly the same as in those reported by Seltzer et al.\(^1\) In terms of the insulin blood sugar reaction described by us,\(^4\) the lowered capacity for the restoration of blood sugar level was constantly observed in the present case, which furthermore showed a persistent low blood sugar level at the intravenous sodium tolbutamide test (Fig. 3) as had been reported by Fajans et al.\(^6\) Seltzer's co-workers. Because of the above features, hypoglycemia was diagnosed in the present case. P.G.T.T. (prednisolone glucose tolerance test) performed on this case further gave the results represented in Fig. 4: fasting blood sugar, 64.3 mg/100 ml; maximal value, 193.1 mg/100 ml at 2 1/2 hours, 46.9 mg/100 ml. The patient fell into a coma while exhibiting the low blood sugar value.

**Table 5. Criteria of early diabetes** (Seltzer)

1) Mild untreated diabetes mellitus is frequently associated with periodic, symptomatic hypoglycemia.
2) Symptoms of hypoglycemia occurring three to five hours after meals represent the earliest clinical manifestation in 110 cases of mild diabetes.
3) G.T.T. as evaluated by Somogyi-Nelson's method on venous blood was 100 mg\% or above at 1 hour, 120 mg\% or above at 2 hours, and, thereafter, the blood sugar level declined to 50 mg\% or less.
4) Of the entire cases 52 per cent were positive for familial diabetic history.
5) Evident diabetic heredity was found in 36\% of the cases.
6) Obesity exceeding 20\% of ideal body-weight was present in 34\% of the cases.
7) The incidence of giant baby is high.
The intravenous sodium tolbutamide test and the insulin blood sugar reaction were examined also on the groups of mild diabetics and hypoglycemic patients. No manifest difference was observed in the fasting blood sugar levels. In the intravenous sodium tolbutamide test, the blood sugar decline index and the sensitivity index in the non-treated diabetic group were 0.36 and 0.43; in the treated diabetic group, 0.44 and 0.42; and in the hypoglycemic group, 0.93 and 1.04, respectively. In the insulin blood sugar reaction, the blood sugar decline index and the sensitivity index in the non-treated diabetic group were 19.1 and 17.6; in the treated diabetic group 21.1 and 20.1, respectively. In the hypoglycemic group the blood sugar decline index was indeterminable because no recovery effect was observed, and the sensitivity index was 10.5. The above observations are interesting in that diabetes and hypoglycemia have a similarity in the blood sugar recovery speed. In terms of the stationary value, however, distinct difference was observed as shown in Tables 2 and 4.

Objecting to the diagnostic criteria of early diabetes proposed by Seltzer et al., Traub stated that repeated determinations of the response to G.T.T. for more than a year would be necessary in such cases. He questioned whether there was evident conversion into diabetes of the cases with functional hypoglycemia in the course of a long-term pursuit. Smelo stated that following the administration of 400 to 500 g of carbohydrate to his patients with the identical hypoglycemic syndrome, he found the disappearance of the specific blood sugar curve in G.T.T. tests. On the basis of this finding, he objected to the assumption that the G.T.T. curve with a phase of initial hyperglycemia was an expression of early diabetes.

The fact that intravenous G.T.T. in the present case (Fig. 4) failed to reveal an elongation of the recovery time indicated that oxyhyperglycemia played a part in this case and yielded a blood sugar curve closely resembling the steeple curve in hypoglycemia after gastric operation.

What then are responsible for the sudden fall in the G.T.T. curve? The following factors would be conceivable: 1) delayed liberation of insulin as assumed by Seltzer, 2) abnormal hepatic regulation of blood sugar, and 3) excess insulin secretion following oxyhyperglycemia or hyperglycemia of unexplained origin.

No definite answer to these questions is yet present.

Diagnosis of mild diabetes by means of the intravenous sodium tolbutamide test has recently come to draw attention. This has been elaborately studied by Unger et al. They took 84 per cent of the blood sugar level before the test for the boundary blood sugar level 20 minutes after intravenous sodium tolbutamide injection. On this basis, they found that, in 100 cases of non-diabetic patients and 75 mild diabetics, 96 per cent of the non-diabetics showed values below the boundary level, but 94 per cent of diabetics showed the blood sugar above the boundary level. As for the blood sugar declines after 30 minutes they found blood
sugar levels lower than 77 per cent of the values before the test in 99 per cent of the non-diabetics, while 90 per cent of the diabetics showed levels not lower than 73 per cent of the pre-test values.

In view of the above findings Yamada et al. examined diabetics in this country. He found that the rate of blood sugar decline in diabetics was slow, the blood sugar decline 20 minutes after tolbutamide administration being 20 per cent of the pre-administration level. Even after 30 minutes blood sugar decline was 23 per cent or lower. Two patients did not show such a slow blood sugar decline, each at one of the two different time intervals mentioned above. In none of the total patients blood sugar decline was larger at the both time intervals than the above values. In my own experiences in mild diabetics, however, one of the patients exhibited blood sugar decline of 21.4 per cent and 28.5 per cent at 20 minutes and 30 minutes, respectively, as presented in Table 1 and Fig. 5. The G.T.T. in this case showed a diabetic curve, i.e., fasting blood sugar, 93.9 mg/100 ml; maximal value, 207.0 mg/100 ml; and at 2 hours, 121.8 mg/100 ml. Thus, the blood sugar declines at 20 and 30 minutes in tolbutamide tests do not always permit of diagnosing diabetes. The diagnosis of very early diabetes is a matter that requires further studies.

The G.T.T. readings at 2 to 3 hours alone do not necessarily permit of the diagnosis of early diabetes. In the present case, examinations for at least five hours were necessary. When the G.T.T. is carried out in the way as was proposed by Seltzer et al., it appears to be a very useful aid for the diagnosis of early diabetes, and the follow-up of the present case will be continued for a still longer period.

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References