THE CONSTITUTIONAL HYPERBILIRUBINEMIA IN JAPAN
STUDIES ON THE 139 CASES REPORTED DURING
THE PERIOD FROM 1963 TO 1969

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Summary

Statistical observations were performed in 139 cases of constitutional hyperbilirubinemia which were reported during 7 years from 1963 to 1969 in Japan. Male was predominant in Dubin-Johnson syndrome (Dubin-Johnson), but there was no difference with sex in Rotor's type of hyperbilirubinemia (Rotor) and Gilbert's disease (Gilbert). The age, at which jaundice first noticed, was distributed in the youngest among patient with Rotor, and age was young in Rotor, Gilbert and Dubin-Johnson as in order. The mean total bilirubin level in serum showed the highest value in Rotor and it showed higher in Dubin-Johnson than in Gilbert. Abnormal retention of BSP a 45 minutes was observed in 80% of Dubin-Johnson and in all cases of Rotor. The secondary rise of BSP in serum was observed in almost all cases of Dubin-Johnson during from 120 minutes to 180 minutes after an injection. Of other liver function tests there were no common changes. Of cholecystography one third of the cases in Dubin-Johnson demonstrated a visualized gallbladder both on oral and intravenous method, while in Rotor the positive rate increased on oral method more than on intravenous method. The black colored liver and the lipofuscin-like pigments in liver cells were observed in all patients of Dubin-Johnson, except patients with hepatic inflammatory changes. In Rotor and in Gilbert the pigments were observed in several patients.

The statistical investigation of constitutional jaundice in Japan was performed by Masuda [1] in 1962.

On Gilbert's disease (Gilbert) new findings were reported by Arias [2], Schmid [3], Billing [4] and others.

Regarding Dubin-Johnson Syndrome (Dubin-Johnson) Mandema [5] reported on the characteristic change of Bromsulphthalein (BSP) concentration in serum after a single injection. Hunter [6] reported on the mobilization of lipofuscin-like pigments in liver cells due to hepatitis in Dubin-Johnson. The visualization of gallbladder on cholecystography in Dubin-Johnson and Rotor type (Rotor) of hyperbilirubinemia was also discussed.

With these points the new statistical observation of constitutional jaundice in

Key word: Dubin-Johnson syndrome, Rotor's type of hyperbilirubinemia, Gilbert's disease, Constitutional hyperbilirubinemia.
Japan was interested and the results of this work have contributed to the clarification of the characteristics of constitutional hyperbilirubinemia.

**Materials and Methods**

The investigation card was sent to doctors who had reported on Gilbert, Dubin-Johnson and Rotor, which appeared in the Journal of Japanese Society of Internal Medicine (Vol. 52, No. 1 to Vol. 58, No. 12) and the Japanese Journal of Gastroenterology (Vol. 60, No. 1 to Vol. 66, No. 12) from January 1963 to December 1969. The authors successfully gathered up 139 cases; 79 cases of Dubin-Johnson, 38 cases of Rotor and 22 cases of Gilbert.

**Results**

A. **Clinical Findings**

1. **Sex (Table 1)**

   There were 59 (74.7%) male cases and 20 (25.3%) female cases in 79 cases of Dubin-Johnson. Male was predominant.

   There were 20 (52.6%) male cases and 18 (47.4%) female cases among 38 cases of Rotor, and there were 10 (45.5%) male cases and 12 (54.5%) female cases among 22 cases of Gilbert. There was little differentiation of frequency between male and female in the occurrence of Rotor and Gilbert.

<table>
<thead>
<tr>
<th>Table 1. Number and sex of reported cases</th>
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<tr>
<td>Dubin-Johnson</td>
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<td>----------------</td>
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<tr>
<td>Sex</td>
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<td>No.</td>
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<td>Total</td>
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2. **Age (Fig. 1)**

   The age, at which jaundice first appeared, was distributed between 8 years old and 65 years old. Among patients with Dubin-Johnson the highest percentage (69.6%) distributed from 11 to 20. The percentage from 1 to 10 was 15.1%, and from 21 to 30 was 8.8%.

   In Rotor the patients between the ages of 1 to 10 occupied the largest percentage (55.2%), which was over the half of the total patients; patients aged from 11 to 20 was 36.8%; from 21 to 30 was 7.8%. The percentage of patients aged from 1 to 20 was 92.0%, and there was no case in which the onset of the disease occurred at an older age than 31 years old.

   In Gilbert the largest percentage (40.9%) was occupied by the patients aged from 11 to 20; age 1 to 10 was 31.8%; 13.6% of the patients aged from 21 to 30. The percentage of onset of the disease in the 4th, 5th and 6th decade was 4.5% respectively. The percentage of onset of Gilbert in the patients younger than 20 years old was 72.7% and this percentage was the lowest rate compared with that of Rotor and Dubin-Johnson. It was also characteristic that Gilbert was found in the advanced aged.