HYPERTROPHY OF PAROTID GLANDS IN DIABETES MELLITUS
AND INTERNAL SECRETION OF SALIVARY GLANDS

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It is well known since Hippocrates that orchitis is one of the complications in mumps. Mohr (1), Nagel (2), Flaum (3) and H. J. John (4) advocated the theory of explaining the salivary glands as internal secretory organs after recognizing clinically that hypertrophy of parotid glands is a common symptom in hormonal diseases, but their theory was based merely on few case-reports and lack experimental criteria. Furthermore, Goljanitzki (5), Mansfeld (6), Uchitnura (7) and Ogata (8) discussed the theory of internal secretion of salivary glands, illustrating the results of their animal experiments, but it must be noted there are many discrepancies in their results.

Accordingly, it can be assumed that no one has yet established the theory of internal secretion of salivary glands both clinically and experimentally.

Because of extreme shortage of insulin in Japan during 1946, Takaoka applied, instead of insulin treatment, X-ray irradiation on thyroid glands of diabetic patients. In February 1947, Takaoka noticed for the first time the symmetrical and non-inflammatory swelling of bilateral parotid glands in a young diabetic patient whose symptom was exacerbated during the daily irradiation. After observing the similar hypertrophy of parotid glands of two other diabetics successively in March and May, we started to make a research on the theory of internal secretion of salivary glands. This report is to describe the gist of our research.

1. Results of palpation of parotid glands

Methods of the palpation of the parotid glands is to hold the subcutaneous tissue directly under the ear-lobe by thumb and forefinger as seen in Photo 1 and to close the space between two fingers carefully. Then the peculiar hardness of the parotid glands can be felt deep inside therein. Up to now total number of persons examined by this method is 3,638. With the exception of intensive edema or tumor infiltration there is no difficulty in palpation. When parotid glands may be palpable only on one side, we take it, too, as positive parotid glands.

Result of the palpation on 2,276 normal individuals disclosed that approximately 15 per
cent of them were positive regardless of age with the exception of girl's high school where 35.5 per cent of students were positive. There was no close correlation between anamnesis of mumps and hypertrophy of parotid glands. In obese persons, however, palpable salivary glands were usually found in high percentage, as Sprinzels (9) stated.

In our clinic, 26.8 per cent of 376 hospitalized patients of various diseases were positive, while 43 out of 44 persons in the latter half of pregnancy, 79 out of 94 diabetics and 9 out of 10 Grave's disease were confirmed to be positive. This fact shows that the positive rate in hormonal diseases is higher than 80 per cent. Moreover, we found that in diabetics submaxillary glands are often simultaneously hypertrophic. According to our, long time observation of diabetics, the parotid glands are remarkably swollen and hypertrophic in improved stadium of the main disease and atrophic or unpalpable in impaired stadium. This was true in cancer patients, too. We could confirm such variations during the insulin treatment of diabetics.

From these findings we consider it is advisable to call the hypertrophy of parotid glands of normal individuals as “simple hypertrophy of parotid gland” and to call hypertrophy in hormonal diseases as “Takaoka's sign”

2. Sialography

The instillation of 2 cc of 30 per cent Solution of moljodol into parotid glands through Stenon's duct by washing apparatus of lacrimal duct brings swelling of the parotid glands and its branched ductulus can be seen clearly by X-ray photography. This sialographical findings leave no doubt that it is nothing other than parotid glands what we have palpated so far.

3. Histological findings

Average weight of parotid glands of 70 autopsy cases of various kinds of diseases performed in the Department of Pathology of Tokyo University was 17.1 grams. In almost all of the persons with positive parotid glands the weight was heavier than the average. Furthermore, in three diabetics who died of complications, either “Streifenstück” (Zimmerman 1927) or acinus cells were atrophic and in one case of coma diabeticum, both of them were atrophic.

We also examined parotid glands of 4 diabetic patients by biopsy. In three mild cases we recognized distinct hypertrophy of “Streifenstück” and great deal of zymogen granule in acinus cells. But in one severe case there was no such finding. These findings coincide with the results of palpation.

4. Results of extirpation of the salivary glands in alloxan diabetic dogs. (Table 1)

The studies were performed on active principles extracted from extirpated salivary glands of 5 alloxan diabetic dogs after maintaining their blood sugar level normal for two months. The dog No. 15 died 9 days after the time of alloxan injection. As dogs Nos. 19, 20 and 21 were fed with irregular diet and treated by treated by insulin, sugar tolerance test to see the difference before and after the extirpation of salivary glands could not be performed. As dog No. 9 had suffered only transitory glycosuria without insulin treatment and after 45 days sugar tolerance test showed improvement to the
normal level before the alloxan injection, then we extirpated the whole salivary glands. Immediately after the extirpation we observed impairment of sugar tolerance function. (Fig. 1)

Next, on each of all salivary glands extirpated from No. 9, No. 15 and No. 20 insulin-extracting method developed by Best, Jephcott and Scott was applied. Each solution thus obtained proved to lower fasting blood sugar level of normal rabbits by 30 per cent. (Fig. 2).

Moreover, the alcohol- and ether-extracts of parotid glands of dogs 19 and 21 showed the same effect, even though they were slighter than the former (Fig. 2).

Table 1. Blood sugar reducing effects of salivary glands and liver in normal dogs and alloxan diabetic dogs.

<table>
<thead>
<tr>
<th>No. of dogs</th>
<th>Alloxan diabetic dogs</th>
<th>Normal dogs</th>
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<tbody>
<tr>
<td></td>
<td>Salivary glands</td>
<td>Liver</td>
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<tr>
<td></td>
<td>(i) (ii) (iii) (iv)</td>
<td></td>
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<tr>
<td>Dose of alloxan injected (mg/kg)</td>
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<td></td>
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<tr>
<td>Body weight (kg) prior to extirpation</td>
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<tr>
<td>Body weight at the time of extirpation</td>
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<tr>
<td>Body weight at the time of death</td>
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<tr>
<td>Survival time (days)</td>
<td></td>
<td></td>
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<tr>
<td>Materials for extraction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parotid gland</td>
<td>4.2 — 11.0 7.5 16.0 — — —</td>
<td>Pt of 3 dogs</td>
</tr>
<tr>
<td>Submaxillar gland</td>
<td>8.0 — 12.3 17.5 21.0 — — —</td>
<td>14.0 9.5 10.5</td>
</tr>
<tr>
<td>Total</td>
<td>12.0 10.5 23.3 25.0 37.0 60.0 60.0 60.0 15.0 21.0 15.4 18.0</td>
<td></td>
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<tr>
<td>Method of extraction</td>
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| B. J. S.; Method of insulin extraction developed by Best, Jephcott and Scott. al.; alcohol extraction and E.; lipid removal by ether.
Initial blood sugar value is estimated as 100.

Fig. 2. Influence upon fasting blood sugar of normal rabbits of parotid gland extracts from dogs.

As a control, the same extracting method was applied on the liver of said dog Nos. 19, 20, 21, (Fig. 3) and on salivary glands of 4 normal dogs (Fig. 2). The results indicated that the extracts contained no blood sugar reducing principle.

**Summary**

1. The parotid glands were palpable in about 15 per cent of normal persons and in over 80 per cent in hormonal diseases.
2. The parotid glands in diabetics are remarkably hypertrophic in improved stadium of the main disease and atrophic in impaired stadium.
3. We have now succeeded in extracting of the blood sugar reducing substance from salivary glands of 5 alloxan diabetic dogs and in producing the falling-off phenomenon of salivary glands in one case.
4. We believe these facts indicate that the salivary glands as internal secretory organs play a compensatory role to pancreas in regard to carbohydrate metabolism.

**References**