Studies on the Action of Saliva.

III. Effects of the Extirpation of the Salivary Glands on the Secretory Activity of the Gastric Peptic Cells.

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NAKAO found a remarkable increase of histamine in the blood and various pathological changes in the gastric mucosa resulting from the extirpation of the parotid glands of rats. This gave a new significance on the salivary hormone theory of OGATA. NISHI proved that if the submandibular and sublingual glands are extirpated, a lesser increase of histamine in the blood and a slight change in the gastric mucosa can be seen. However, a few peculiar changes in this case are noticeable in the gastric mucosa. He proved also that the changes resulting from the extirpation of the parotid glands can be controlled by the subcutaneous injection of human parotid saliva obtained aseptically or of potato-juice, both of which have a remarkable anti-histamic activity. However again, a few changes resulting from the extirpation of the submandibular and sublingual glands are not decreased by these injections. He also proved that parotid saliva will be different from submandibular saliva in its effect as a hormone.

The authors attempted to prove the change of the secretory activity of the gastric peptic cells which is closely related to histamine in the blood as mentioned above.

I. Materials and Methods.

Adult and male rats accustomed to a regular feeding of McCOLLUM's artificial diet were separated into two groups. In one group, the parotid glands were chirurgically extirpated and in other group, the parotid, submandibular and sublingual glands were extirpated. The rats were fed with an artificial diet for 30 days after the operation and the following experiments were performed.

1. Human parotid saliva obtained aseptically using the method of UMEMOTO and KAKUDO (described below as Saliva) was injected subcutaneously every morning and evening, 0.5 cc each time.

2. Solution (1 cc) of aceton sediment obtained from raw potato juice (described below as Potato-juice) was injected subcutaneously every day. Concerning the solution, see Arch. hist. jap. Vol. 12, No. 2 (1957), p. 185—200.
3. 0.5 mg of Restamine, an anti-histamic preparation of KOWA Chemical Factory, was injected subcutaneously every morning and evening.

As the controls, the following were used; 1. normal rats fed with an artificial diet, 2. rats fed for 30 days after the extirpation of the parotid glands, 3. rats fed for 30 days after the extirpation of the submandibular and sublingual glands and 4. rats fed for 30 days after the extirpation of the parotid, submandibular and sublingual glands.

Samples were taken on the 31st day at periods of 1. before administration of the diet and 2. ¼, 1, 1¼, 2, 3 hrs. after the diet. Under ether narcosis, LUNA's liquid was injected into all arteries through the left heart ventricle for the vital fixation. Small pieces were taken from the glandular portion of the stomach, and they were placed in KOLSTER's liquid for the post fixation. Serial paraffin sections of 4 μ were made and stained by HEIDENHAIN's iron haematoxylin.

II. Observations and Discussion.

The representative results of each case are shown briefly in the figures. As regards indication of the quantity of secretion granules and vacuoles in the peptic cells, the usual method of our laboratory was used, viz. secretion granules or vacuoles filled in the upper half of the cell were marked +++, no granule or vacuole in the cell was marked −, and three intervening steps of +++, +, ±, were made suitably between +++ and −. For the productin vacuoles in the surface cells, filled vacuoles in the under half of the cell body were marked +++, no vacuole was marked −, and similar intervening steps as above were made between them. Concerning these, see FUJIKI: Arch. hist. jap. 18 (1959).

1. Extirpation of the parotid glands, of the parotid, submandibular and sublingual glands and of the submandibular and sublingual glands (Fig. 1 and 2).

The observations obtained from the extirpation of the parotid glands and from that of all salivary glands were so similar that the authors describe only the former.
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in Fig. 1. While rats are still unfed, numerous secretion granules and short rod shaped, guitar formed or supra-short rod shaped plastosomes (pls.) are seen. After administration of the diet, discharge of productin from the surface cells is almost normal, secretion granules in the peptic cells are produced copiously and vacuolization of the granules is slight. The secretory activity of the cells is still remarkable even at a period of 3 hrs. after the diet.

In case of the extirpation of the submandibular and sublingual glands (Fig. 2), peptic secretion granules are numerous, most of pls. are short rod or supra-short rod in unfed rats, but at a period of ½ hr. after the diet, secretion granules decrease and secretion vacuoles increase in the cells and long rod shaped pls. are numerous. 1—2 hrs. after the diet, secretion granules increase again in the cells and pls. transform into active form but vacuolization of the secretion granules is still noted. 3 hrs. after the diet secretory activity of the peptic cells seems to be low. It is noticed in this case that secretion vacuoles increase in the cells after the diet more speedily than those in the normal case (Fig. 3).

It was previously proved by SHIMIZU that production of peptic secretion granules was promoted by histamine or the gastric hormone productin and that vacuolization of the granules was by the decomposed product of histamine or of productin.
On the other hand, FUJIE proved the anti-histamic action of parotid saliva. Therefore the results shown in Fig. 2 will be explained by the increased anti-productin activity in vivo resulting from the compensative remarkable secretion of the parotid glands in turn caused by the absence of the submandibular and sublingual glands.

From the results obtained from the peptic cells (Fig. 1 and 2), it may be concluded that parotid saliva does have an anti-productin activity and that submandibular saliva does not.

2. *Saliva, Potato-juice or Restamine was injected for 30 days after the extirpation of the parotid glands* (Fig. 4, 5 and 6).

If *Saliva* was injected subcutaneously every morning and evening (Fig. 4), vacuolization of peptic secretion granules is more remarkable than in case of non injection (Fig. 1). Transformation of pls. is slight.

If *Potato-juice* is injected (Fig. 5), temporary remarkable vacuolization of peptic granules can be seen 1 hr. after the diet, but accumulation of the granules in the cells 1½—3 hrs. after the diet is almost identical with that in case of non injection.

In *Restamine* injection (Fig. 6), vacuolization of peptic secretion granules is
Comparing the above three cases, it is discernible that the abnormality of secretory activity in the peptic cells resulting from the lack of the parotid glands decreases considerably with the injection of Saliva, but not completely so as far as the present authors tested (0.5 cc of Saliva each time), and that the effect of Potato juice is also considerable but not continuous, and that Restamine is less effective. The lesser effect of Restamine than those of Saliva and of Potato-juice is coincidental with the result of NISHI obtained from the pathological changes of the gastric mucous membrane.

3. Saliva, Potato-juice or Restamine was injected for 30 days after the extirpation of all salivary glands (Fig. 7, 8 and 9).

In the cases of Saliva (Fig. 7) and Potato-juice (Fig. 8), secretion vacuoles in the peptic cells are generally fewer than those in case of the extirpation of the parotid glands alone, and the vacuoles increase a little in the cells more than 1 1/2 hr. after the diet. Viz. the effect of Saliva or of Potato-juice on the vacuolization of peptic granules seems to be delayed in this case. The transformation of pls. is active after the diet. Short rod shaped, guitar formed or short rosary formed pls. increase
in the cells.

In case of Restamine (Fig. 9), a continuous and active vacuolization of peptic granules can be noticed after the diet. The transformation of pls. is already not so active at period of 3 hrs. after the diet.

The secretory abnormality of the gastric peptic cells resulting from the extirpation of all salivary glands can be decreased more effectively by the injection of Restamine than by the injection of Saliva or Potato juice. Here is the big difference from the case of the extirpation of the parotid glands. NISHI proved previously that Restamine can not inhibit the pathological changes of the gastric mucous membrane caused by the extirpation of the parotid glands and that Restamine is considerably effective on the inhibition of the pathological changes of the gastric mucosa caused by the extirpation of the submandibular and sublingual glands. There seems to be something in common between the results of NISHI and of the authors.

As a result of these observations, it is noticed that parotid saliva is different from submandibular saliva in its action and that the actional difference between them is due to their component differences.
III. Summary.

The effects of the extirpation of the salivary glands on the secretory activity of the gastric peptic cells were investigated.

1. After the extirpation of the parotid glands or of the parotid, submandibular and sublingual glands, production of secretion granules in the peptic cells is copious and is prolonged for a long period after administration of the diet, and vacuolization of the granules (discharge of the granules) is very inferior.

2. After the extirpation of the submandibular and sublingual glands, remarkable vacuolization of peptic secretion granules can be seen ½—1 hr. after the diet.

3. If human parotid saliva obtained aseptically is injected subcutaneously every morning and evening after the extirpation of the parotid glands, considerably remarkable vacuolization of peptic granules continues for a long term after the diet. If potato-juice is injected every day, vacuolization of the granules is remarkable but is not continuous. If Restamine is injected, a little more remarkable vacuolization than that of the control (non injected) is noted.

4. If the same injections as above 3. are tested after the extirpation of the parotid, submandibular and sublingual glands, it is noticed that vacuolization of peptic granules increases only a little 1 ½—3 hrs. after the diet in case of injections of Saliva or of Potato-juice, and that vacuolization of the granules is continuous after the diet in case of injection of Restamine. The latter is similar in tendency to that obtained by the injection of Saliva after the extirpation of the parotid glands.

From these results, we may say that parotid saliva is different from submandibular saliva as regards its anti-productin activity and that this difference seems to be due to its essential components.
References.