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On the Images of Endocrine Function in the Surface-cells of the Gastric Mucous Membrane.

胃粘膜表在細胞の内分泌像に就て.

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FUJIE, one of the authors, has previously found that the substance which stimulates haematogenously the production of secretion granules in the peptic and pancreatic cells, exists in the mucous membrane of the stomach, and he suggested the substance be name "productin". And he also recognized that this substance was histamine or a histamine-like substance and its decomposed substance decomposed while circulating with blood, has an action, which stimulates the discharging of the secretory substance in the peptic cell, i. e. so called gastrin-like action. In this connection it was known that the gastrin theory, suggested by EDKINS in 1906, is a theory established upon the facts which could be recognized as a result, and from the consideration of the process of the secretion of gastric juice, especially of the series of functional movements of the gland cells, this theory was only applied to the second half of the secretion process and the first half of it was initiated by productin (this Arch. Vol. 3, No. 4, P. 403). It is a well known fact that the secretory phenomenon is performed by the cells which have secretory function. Therefore, if a substance is secreted from the gastric mucosa, the cells which have the secretory function, must be found in the mucosa.

The authors fixed their eyes upon this point and commenced the study to search for such cells which show secretory function, besides the previously well known gland cells in the gastric mucosa.

I. Materials and Methods.

The experimental animals are mature rats which have been accustomed to constant and regular feeding of artificial food. And 24 hrs. after the last feeding, the authors performed the experiments as follows.

1. Oral administration of sesame oil with a sonde, then $1\frac{1}{2}$, 1, $1\frac{1}{2}$ and 2 hrs. later, materials were taken.

2. Oral administration of sesame oil with a sonde after ligation of the pylorus, then materials were taken $1\frac{1}{2}$, 1, $1\frac{1}{2}$ and 2 hrs. later.

3. Injection of a gastric extract 0.5, 1.0 and 1.5cc. Then materials were taken 20 and 40 min. after the injection.
4. Subcutaneous injection (1cc) of histamine solution. 0.1, 0.3, 0.5 and 1.0%. Materials were taken 20, 40 and 60 min. after the injection.
5. Same method of administration of acetylcholin solution.
6. Injection of a duodenal extract (0.5cc., 1.0cc.). Then 20 and 40 min. after the injection. materials were taken.

Several pieces were taken from the corpus ventriculi, some of them were placed in KOLSTER's and LEVI's liquid and used for the research of the minute structure of the cell, some were placed in CIACCIO's liquid and Formalin solution for the purpose of fat-staining, and others were placed in CARNOY's liquid and used for glycogen research.

II. Observation.

There are no cells which can be considered as having a secretory function in the gastric mucosa except the three kinds of cells in the gastric glands. But in the epithelial cells of the gastric surface, a possibility of that function can be presumed, too. Therefore the authors performed the first research on the gastric epithelial cells.

A. Control (figs. 1—3).

At 24 hrs. after the last administration of artificial diet, the epithelial cells of the gastric surface are cylinder shaped and the nucleus is located in the center or the upper part of the cell body as shown in figs. 1—3. Plastosomes (pls.) are distributed almost to all parts of the cell body but in the upper of the nucleus, some tendency to crowd can be seen. They are granular, short rod or long rod shaped, and many granular ones are located in the upper part of the nucleus, many rod shaped ones are in the side part of the nucleus and the lower part of the cell body.

Here, the most important fact is that the epithelial cells do not always show a typical representation of a cylinder-epithelium as it is shown in fig. 1, but the cells which contain many or large vacuoles in the basal portion of the cell body as shown in fig. 2 or 3, are not few. And these vacuoles are always seen from the subnuclear part to the basal portion of the cell and it is not seldom that the cells show an abnormal corpulence because of the accumulation of vacuoles (fig. 3 left) and in some cases the vacuoles in the cells connect with the vacuoles in the propria mucosae (like in fig. 10 right).

The results of fat staining (Sudan III, and Scarlet red) or glycogen-staining (BEST's carmine) are all negative and it is almost certain that the content of these vacuoles are neither fat nor glycogen.

B. Administration of sesame oil (figs. 4—6).

30 min. after sesame oil administration, the epithelium of the gastric surface seems a typical cylinder epithelium, but with more careful observation, many cells which contain little vacuoles in the base of the cell as shown in fig. 4, are recognized. Pls. are granular in the apical portion of the cell and rod-shaped in the side part of the nucleus and the lower of the cell body.

60 min. after administration the cells, containing vacuoles in the base of the cell body (like in fig. 4), are few, and the epithelium consists of such cells as shown in fig. 5. That is, most of the pls. are short rod shaped or long rod shaped and many short rod shaped ones are in the apical portion of the cell. However, at 1.5 hrs. and 2 hrs. after administration pls. are granular in the apical portion and short or long rod-shaped in the basal portion of the cell. On the other hand, the cells which contain small vacuoles in the basal portion of the cell body or the side portion of the nucleus are recognized (fig. 6), and they seem to increase gradually.

C. Sesame oil administration with ligatured pylorus (figs. 7—9).

30 and 60 min. after sesame oil administration with ligatured pylorus, the cell images of the gastric epithelium are similar with the ones obtained 30 min. after sesame oil administration (experiment B), and also in this case the cells which contain no vacuoles show the images similar to fig. 1. The cells which contain vacuoles in the basal portion of the cell, have a few small vacuoles, as shown in fig. 7.

At 1.5 hrs. after the administration, the cell-images are almost identical to the 60 min. after sesame oil administration ones (fig. 5). However, it is often noticed in this case, that the cells contain a few small vacuoles in the basal portion of the cell body and many granular pls. as it is shown in fig. 8.

2 hrs. after the administration, many cells, shown in fig. 9, are recognized. Pls. are granular in the apical portion of the cell and short or long rod-shaped in the middle and the lower part of the cell body. In the basal portion of the cell, a few, but relatively big vacuoles are contained.

D. Injection of several kinds of medicaments (figs. 10—12).

The medicaments which were used by FUJIE for the other experiments, were also used in this study. That is a gastric extract (0.5cc, 1.0cc), 1cc of histamine solution (0.1%, 0.3%, 0.5%, 1.0%), 1cc of acetylcholin solution (0.1%, 0.3%, 0.5%, 1.0%) and a duodenal extract (0.5cc, 1.0cc). Observation was performed 20, 40 and 60 min. after the subcutaneous injection of those substances. The minute structures of the gastric epithelial cells never change by these injections. Granular Pls. crowd in the apical portion of the cell and rod-shaped ones distribute in the lower

half of the cell body. The cells, containing vacuoles in their basal portion, contain as many vacuoles after injection as before, regardless of the substances injected or of the time elapsed from the injection (figs. 10—12).

The functional movements such as these vacuoles decreasing equally, then increasing gradually and the decreasing of granular pls. etc., which were recognized in the experiment of sesame oil administration, were never observed in these cases. By fat-staining and glycogen-staining, there can be seen no substance stained in the cells.

III. Discussion.

According to the summarization of the observations described above, the epithelial cells of the gastric surface of mature rats often contain many vacuoles in the lower half of the cell body. These vacuoles do not decrease or increase by subcutaneous injections of gastric, duodenal extract, histamine or acetylcholin solutions (figs. 10—12), but they decrease rapidly after administration of sesame oil (fig. 4) and almost disappear after 1 hr. (fig. 5), then increase again in the cell body gradually (fig. 6). When the pylorus was ligatured and then the sesame oil given, the decrease of vacuoles were somewhat slight (figs. 7, 8) and the following increase seems to be relatively rapid (fig. 9). These vacuoles in the cells connect with the ones in the propria mucosae (fig. 10 right) and they exist always from the side part of the nucleus to the basal portion of the cell, never to be observed in the apical portion of the cell.

Therefore it can be considered that they are produced in the basal portion of the cell, discharged from the cell base and are closely connected with the administration of diet.

That the epithelial cells of the gastric surface contain vacuoles was previously reported by Prof. KUROTSU (1932). But his materials were immature rats, used soon after birth. And he demonstrated, with these immature rats, that the vacuoles were nothing else but fat, glycogen or other substances absorbed after lactation, and that when the differentiation of the epithelial cells were finished, i. e. on the 21st day after birth, the vacuoles were never observed.

If the vacuoles which the authors have recognized in the epithelial cells, are absorbed fat, they must increase remarkably after administration of sesame oil, without decreasing. The fact that the vacuoles decrease rapidly after administration of food and then increase gradually, will demonstrate that the vacuoles are not the absorbed substance. On the other hand, that the results of both fat staining by Sudan III or Scarlet red and glycogen-staining by BEST's carmine are all negative, shows the vacuoles are neither fat or glycogen.

The more interesting facts are the functional movements of the peptic

and the pancreatic cells, which have been published by FUJIE et al. By the administration of sesame oil, the remarkable production of secretion granules are already recognized in both the peptic and the pancreatic cells in 30 min. after the administration, regardless of whether they are the normal rats or the rats with ligatured pylori. The production of secretion granules reaches the maximum in 1.5 hrs. after administration, then the functional image returns gradually to the functionally quiet one. These process and the movement of vacuoles in the epithelial cells are quite coincidental; the vacuoles decrease rapidly when production of secretion granules in the peptic and the pancreatic cells is marked, and the vacuoles increase gradually in the epithelial cells if production of secretion granules in the cells ceases.

In the case of gastric extract and histamine injection, the peptic cells and the pancreatic cells present a remarkable image of secretion granule production and it is quite similar to that of sesame oil administration. however, vacuoles in the epithelial cells of the gastric surface show neither increase nor decrease.

According to these results, it can be considered that the action of the injected gastric extract are caused by the substance contained in the vacuoles of the epithelial cells, and the substance has a similar action as that of histamine. Therefore it seems possible that "productin" which FUJIE has previously suggested, may be nothing else but the substance contained in the vacuoles of the gastric epithelial cells. The authors believe so, according to the results of the previous studies, published by FUJIE et al.

IV. Summary.

According to the fact that the substance which stimulates haematogenously the production of the secretion granules in the peptic and the pancreatic cells, is secreted from the gastric mucosa, the authors performed the first research on the epithelial cells of the gastric surface to determine where in the gastric mucosa such a substance is contained and the authors obtained the following results:

1. The epithelial cells of the gastric surface contain many big vacuoles in the lower half part of the cell body.
2. These vacuoles connect sometimes with the ones in the propria mucosae.
3. The vacuoles decrease rapidly toward the cell base after administration of food, then they increase again in the cell, gradually.
4. By injection of gastric extract, duodenal extract, histamine solution or acetylcholin solution, the vacuoles never increase or decrease.
5. The vacuoles are negatively stained by both fat- and glycogen staining.

These results compare with the experimental results published previously

by FUJIE et al., both results are quite coincidental. Hereby the authors believe that the endocrine function of the epithelial cells of the gastric surface exists, and that the secretory substance of that cell must be "productin" which was named by FUJIE.

内 容 自 抄.

著者等は胃粘膜中より血行性に胃腺主細胞及び隣細胞の分泌顆粒新生を刺戟する物質の分泌せられる事実に鑑み、之が粘膜中の何処に含有されて居るかを検索する目的を以て、先づ胃表上皮を検索した処、胃表上皮細胞が胞体の下半部に多数の大空胞を有する事を認めた。この空胞は時に固有層に存する空胞と連結して居り、又給食すると細胞底に向つて急速に減少し、後再び漸次増加する。他方胃粘膜抽出液、ヒスタミン溶液等を皮下注射しても空胞には影響しない。又脂肪、糖原染色では非染色性である。

之等の成績と藤江等が曩に発表した各種の実験成績とを総合すると誠によく一致する点が多く、之によつて著者等は胃粘膜表在細胞の内分泌機能を信じ、この分泌物は藤江の主張する Productin であらうと考える。

References.

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Explanation of Plate.

These figures are reproductions obtained with ABBE's apparatus. All cell images are described under the same magnification.

Figs. 1, 2 and 3. The epithelial cells of the gastric surface of the starved rat. Contain no vacuoles (fig. 1), many vacuoles (fig. 2) and big vacuoles (fig. 3) in the lower half part of the cell body.

Fig. 4. 30 min. after administration of sesame oil. It is believed that the vacuoles such as in figs. 2 and 3 have decreased rapidly.

Fig. 5. 60. min. after administering the same.

Fig. 6. 1.5 and 2 hrs. after administering the same. A few vacuoles appear again in the cell body.

Fig. 7. 60 min. after administration of sesame oil with ligatured pylorus.

Fig. 8. 1.5 hrs. after the same method of administration.

Fig. 9. 2 hrs. after the same method of administration. The cells contain more vacuoles than in fig. 6 (2 hrs. after sesame oil administration).

Figs. 10—12. Many types of the epithelial cells observed after injection of histamine-, acetylcholin solutions, gastric and duodenal extracts. The vacuoles never increase or decrease, regardless of the substances injected or the time elapsed after the injection.

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