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On the Effect of Gastric Hormone "Productin" to the Parietal Cells.

胃壁ホルモン Productin が壁細胞に及ぼす影響に就て.

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FUJIE, one of the authors, has previously demonstrated the endocrine function in the surface-cells of the gastric mucous membrane, has named its endocrine secretory substance "Productin" and has concluded that the true nature of productin is a histamin-like substance (Arch. his. jap. Vol. 3, p. 403; Vol. 4, p. 469). On the other hand, he has also demonstrated with many experiments that productin stimulates haematogenously the production of secretion granules in the peptic and the pancreatic cells and then its discharge from the peptic cell.

In the recent research in which he first injected atropin then administered the diet, he obtained the results that the discharge from the peptic cell, which ought to be controlled by atropin, was not influenced and the production of secretion granules in the peptic and the pancreatic cells was controlled and also the control of the productin-secretion (discharge) of the surface cell of the gastric mucosa was noticeable. According to these results, he reached the conclusion that the influences of productin on the secretory function of both the peptic and the pancreatic cells were further effective than that of the automatic nerves.

Here the authors performed the following study to find the greatest factor which dominates the secretory function of the parietal cell, the principal element in the constitution of the gastric gland, as well as of the peptic cell.

I. Materials and Methods.

Mature rats which were accustomed to constant periodic feeding of artificial food were used as the experimental animal. 24 hrs. after food administration, which is the so called hungry time, the following experiments were performed.

1. Sesame oil (1 cc) was injected into the stomach using a sonde then materials were taken 30, 60 min., 1.5 and 2 hrs. later.

2. Atropinum sulfuricum (0.5 mg, jot down as Atp.) was injected subcutaneously then 10 min. later sesame oil was injected orally into the stomach. Materials were taken as in 1.

3. An extract of the pig's gastric mucosa (0.5 cc) was injected subcutaneously then 20, 40 and 60 min. later, materials were taken.

4. Atp. was injected then 10 min. later Histamin dihydrochlor (0.3%, 1 cc, jot down as Hist.) was injected subcutaneously. After 20, 40 and 60 min. materials were taken.

To take materials, LUNA's liquid was injected cardially for the prae-fixation then the small pieces were taken from the stomach (the glandular portion). They were placed in KOLSTER's liquid for the post-fixation. Paraffin sections of 4μ were made and stained by HEIDENHAIN's iron haematoxylin.

II. Observation.

Though the form of the parietal cells is much different according to the portion of the gastric gland, in the basal portion of the gland, most of the parietal cells show the convenient form to catch it's functional movements. Therefore the following observations will be represented by the parietal cells in the basal portion of the gland.

Experiment 1. Oral administration of sesame oil with a sonde, then 30, 60 min., 1.5 and 2 hrs. later, materials were taken.

The parietal cell of the starved rat is generally dark, has no big granules which seem to be secretion granules, and contains short or long rod shaped plastosomes (pls.) in the cytoplasm. The circumference of the cell is distinguished clearly. Cells opening into the gland lumen are few (fig. 1).

30 min. after the administration of sesame oil, a wide light part is produced in the scope from the center to the apex of the cell body. In the peripheral zone of the cell, granular, guitar formed and short rod shaped pls. exist. Among the granules some big ones can be seen. The apex of many cells opens into the gland lumen which is still narrow, and the wide light part in the cell connects with the lumen (fig. 2). 60 min. later, the light part becomes very wide and many big granules can be seen in the peripheral zone of the cell. Pls. are thick and short and distribute between the big granules. The lumen expands noticeably and the light part in the cell continues into the lumen (fig. 3). 1.5 hrs. later, the big granules and the light part almost disappear and thick short rod shaped and granular pls. are distributed in the cytoplasm. The lumen expands, and the apex of the cell opens into it (fig. 4). 2 hrs. later, the light part becomes wide again and big granules also appear. Most of the pls. are thick short rod shaped,

guitar formed or granular. The apex of the cell opens generally into the lumen (fig. 5).

According to these observations, it is noticed that the production and the discharge of the secretory substance can be seen in the parietal cells soon after the oral injection of sesame oil into the stomach and they are most remarkable at 60 min. The secretory substance is discharged almost completely 1.5 hrs. later and it is produced again 2 hrs. later. The discharge continues during these periods.

Experiment 2. Atp. was injected subcutaneously then sesame oil was injected orally into the stomach.

When Atp. is injected before the oral administration of sesame oil, the functional movement of the parietal cell has a different appearance in comparison with that in experiment 1.

30 min. after sesame oil administration, the light part is still narrow and the greater part of the cell body is occupied by thick rod shaped and granular pls. and a few big granules. The gland lumen is too narrow to distinguish whether the apex of the cell opens into the lumen or not (fig. 6). The cell images of 60 min. and 1.5 hrs. later are almost similar, and in the central part of the cell a somewhat expanded light part and in the peripheral zone many big granules can be seen. Pls. are a few and distribute among the big granules. Their forms are short rod shaped and granular. The lumen expands remarkably, the apex of the cell opens into it and the light part in the cell connects with the lumen (fig. 7). 2 hrs. later, the circumference of the cell is bounded clearly and never connects with the lumen, though the cell contains some light part in its center. Pls. show various forms from long rod to granule, and a few big granules can be seen among them (fig. 8).

The functional image of the parietal cells in this case is generally inferior than that of the former case. Both production and discharge begin gradually and end early. Also the production and discharge image which seems the most remarkable (fig. 7) is clearly inferior than the one of the former experiment (fig. 3).

Experiment 3. An extract of the pig's gastric mucosa was injected subcutaneously.

It has been previously demonstrated that productin is contained in an extract of the mucous membrane of the stomach (Arch. his. jap. Vol. 3, p. 119 and 403). The parietal cells of the starved rats to which the extract was injected, have a wide light part and many big granules 20 min. after the injection. The apex of the cell opens into the expanded lumen. Pls. are thick short rod shaped or granular (fig. 9). 40 min. later the following cells can be seen beside the cells mentioned

above. The big granules are few, most of the cell body is light and granular or guitar-formed pls. localize in the peripheral zone and in the circumference of the nucleus (fig. 10). 60 min. later the cell images are similar to the ones of 20 min.

That is, the functional image of remarkable production and discharge can be seen in the parietal cells of the starved rats, following the injection of a gastric extract, and it reaches the maximum 40 min. after the injection. This maximum-image can be said to be a more remarkable one than that which has been recognized in experiment 1.

Experiment 4. Hist. was injected after the injection of Atp.

Atp. was injected into the starved rats, then 10 min. later Hist. was injected. 20 min. after the injection of Hist. a remarkable corpulence can be recognized in all parietal cells and most of the cell body consists of the light part. Only in the cell base, a few protoplasm with granular and supra-short rod shaped pls. can be seen. The lumen is narrow but the apex of the cell opens into it (fig. 11). 40 min. later, the expansion of the lumen is marked, the light part of the cell body becomes somewhat narrow but it still occupies the majority of the cell body. In the peripheral zone of the cell big granules and short rod shaped or granular pls. are distributed (fig. 12). 60 min. later, big granules are few and thick rod shaped, guitar-formed and granular pls. distribute. From the center to the apex of the cell the light part can be seen and it connects with the narrow lumen (fig. 13).

As in this case, when Atp. then Hist. is injected, the control action of Atp. as it has been recognized in experiment 2, is never recognized and the parietal cells show a remarkable functional image. The cell image as shown in fig. 11 seems to be an abnormally marked production of the secretory substance and a more remarkable function than the cell image (fig. 10) which was recognized 40 min. after the injection of a gastric extract.

III. Discussion.

From the observations of the parietal cells, it is noticed that the functional movements are clearly different according to each experiment. It is very interesting to observe the functional movements of the parietal cells alone. But it is more interesting if the movements of the parietal cells are compared with the endocrine function of the surface cell in the gastric mucous membrane, because it seems that the cause which makes the differences in the function of the parietal cells can be understood. After the oral administration of sesame oil into the starved rats, many vacoules in the subnuclear part of the surface cells of the gastric mucosa decrease rapidly, and 30 min. later the

majority of them and 60 min. later almost all disappear. After 2 hrs. the vacuoles reappear gradually in the same portion (Arch. his. jap. Vol. 4, p. 291). In the comparison of this observation with the parietal cells of experiment 1, the decrease of the vacuoles in the surface cells and the production of the secretory substance in the parietal cells are very coincidental to each together.

On the other hand, if Atp. is injected before the sesame oil administration, the vacuoles in the subnuclear portion of the surface cells decrease a little 30 min. later but at 60 min. later they begin to increase again and 2—3 hrs. later revive into the filled state as before the injection (Arch. his. jap. Vol. 5, p. 185). Therefore it can be said that the amount of productin discharged is small in this case. The parietal cells in this case are shown in figs. 6, 7 and 8. The function is inferior and slight production and discharge can be seen but they end early, i.e. the function of the parietal cells are inferior when discharge of productin is less active. However, the discharge which ought to be controlled by Atp. by general consideration, is initiated with no effects by the Atp. Also if the peripheral part of the parasympathetic nerve in the parietal cell is narcotized, the condition is the same as a sympathicotonic one, so that even if the discharge is controlled the production should be initiated remarkably well as in the case when it is not atropinized. But these are also not recognized. Therefore it can be considered that the inferior function of the parietal cells, mentioned above, is not the direct result of Atp. but the result of atropin controlling the discharge of productin in the surface cells of the gastric mucosa.

Here, with the results of experiment 1 and 2, it is clear that the function of the parietal cell is dominated further effectively by productin than the automatic nerves. In this point, the functions of the parietal cell, as well as the peptic and the pancreatic cells, are dominated by the same stimulus.

These consideration are also demonstrated by the results of the injection of a gastric extract (exp. 3, figs. 9 and 10) and the injection of Atp. then Hist. (exp. 4, figs. 11, 12 and 13). If a gastric extract is injected into the starved rats, the functional images of the parietal cells are similar to that of sesame oil administration and it is more marked than the latter. If Atp. then Hist. are injected, the parietal cells show the images of remarkable production and discharge similar to the ones followed by the injection of Hist. alone (Arch. his. jap. Vol. 3, p. 410), and a image where it seemed to be controlled by Atp. can not be recognized. Therefore it is not doubtful that the parietal cell produces the secretory substance then discharges it owing to an action of productin.

The cell image which can be seen 20 min. after Atp. and Hist. injections (exp. 4, fig. 11) show further remarkable production than the case of Hist. alone. For this observation, there can be several considerations. For instance, as the individual difference of the sensibility for Hist., or as the synergistic action of Hist. and the sympathetic nerves in promoting the production, because the peripheral part of the parasympathetic nerves are anaesthetized by Atp.

However it may be, that the function of the parietal cells are dominated greatly by productin is a certain fact. The authors do not ignore the influences of the automatic nerves but that the nervous influences are not recognized in the peptic and the pancreatic cells except in special case as stimulation by electrically etc., was often demonstrated in FUJIE's previous studies. In this research the authors found that the parietal cell was also not an exception.

Though the peptic and the parietal cells are dominated by the same factor, productin, the lapse of the functional performance is somewhat different between them. The production of the secretory substance is performed almost at the same time but the discharge is always faster in the parietal cell than in the peptic cell. And in the parietal cell, observed at intervals of 20 or 30 min. after the experiment, not only the image of production but discharge, though the latter is still inferior, can be recognized. This will be due to the difference in the sensibility of the cell-itself, but on this detail there seems to be room for further investigation.

IV. Summary.

In order to find the factor which dominates the function of the parietal cell, the authors performed the experiments of administering sesame oil orally into the starved rats (exp. 1), of administering sesame oil after the injection of Atp. (exp. 2), of injecting subcutaneously an extract of the gastric mucosa of the pig (exp. 3) and of injecting Atp. then Hist. (exp. 4).

After administration of sesame oil, production of the secretory substance becomes remarkable in the parietal cell, big granules and the wide light part appear. On the other hand, the apex of the cell opens into the lumen and the cell shows the function of discharging the secretory substance. Both discharge and production reach the maximum 60 min. later. After this the secretory substance is discharged completely and produced again continuously. These functional movements, especially the productive functions, are very interesting because they are quite coincidental with the movements of the productin-vacuoles in the surface cells of the gastric mucosa.

However if Atp. is injected before sesame oil administration, the functional images of the parietal cells, both production and discharge, are less active and end early. The productin-vacuoles of the surface cells in this case decrease a little and soon increase again. According to these observations it is considered that the function of the parietal cells is dominated greatly by productin. This will be demonstrated more certainly by following two results, that the parietal cell shows the similar remarkable movements to the ones following the administration of sesame oil after the injection of a gastric extract (exp. 3) and that it shows a very marked production and discharge after the injection of Atp. and Hist. (exp. 4).

By addition of the results obtained here, to the ones which have been obtained previously by FUJIE, the authors reached the following conclusions:

1. The greatest factor dominating the function of both the peptic and the parietal cells in the gastric gland is productin, secreted from the surface cells of the gastric mucous membrane into the blood.
2. The automatic nerves give greater influences to the productin-secretion in the surface cells rather than to the secretion in the gastric gland cells.

内 容 自 抄.

著者等は胃腺壁細胞の機能を支配する因子を探究すべく空腹ラッテにゴマ油の胃内注入(実験1), Atropin を注射した後ゴマ油を注入(実験2), 豚胃粘膜抽出液を皮下注射(実験3), Atropin を注射した後 Histamin を注射(実験4)の4実験を行った。

ゴマ油を注入すると、壁細胞には分泌物新生、放出が旺盛となり、60分後を極として再び平靜にかえる。この機能的動態就中新生機能の動きは胃粘膜表在細胞に於ける Productin 空胞の消長とよく一致する点に於て甚だ興味深い。

処が予め Atp. を注射しておくと、壁細胞機能像は新生、放出共低調で、而も早く終了する。此時胃粘膜表在細胞では Productin 空胞は一時少々減少するが、再び増加し充満するに到る。斯る所見より壁細胞機能は Productin によって大きく影響されることが推察される。之は更に胃粘膜抽出液を注射すると壁細胞はゴマ油注入後と類似の而もより旺盛な機能像を示すこと及び Atp. 注射後 Hist. を注射すると非常に旺盛な新生及び放出像が現われることの2つの成績によって一層明確にされる。

著者等は之等の成績を藤江の龔に得た成績に追加して、1 胃腺主細胞及び壁細胞の機能を支配する因子の主たるものは胃粘膜表在細胞より内分泌

せられる Productin であること, 2. 自律神経は之等胃腺細胞に対するよりも寧ろ胃粘膜表在細胞の Productin 分泌機能に対して大なる影響を与えること, を結論することが出来る.

References.

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Explanation of Plate.

These figures are the reproductions obtained with ABBE's apparatus, under the same magnification.

Fig. 1. The parietal cell of the starved rat.

Figs. 2, 3, 4 and 5. 30 and 60 min., 1.5 and 2 hrs. after the oral administration of sesame oil.

Figs. 6, 7 and 8. The oral administration of sesame oil after the subcutaneous injection of Atp. 30 min., 60 min.—1.5 hrs. and 2 hrs. later.

Figs. 9 and 10. 20 and 40 min. after the subcutaneous injection of an extract of the pig's gastric mucosa.

Figs. 11, 12 and 13. The subcutaneous injection of Hist. after the one of Atp. 20, 40 and 60 min. later.

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