**Histological and Histochemical Investigations on the
Stomachs in Man, Japanese Monkey (*Macaca
fuscata yakui*) and Some Other
Kinds of Animals**

**Report I. Cell-divisions in the Gastric Glands in Man,
Japanese Monkey and Dog**

By

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The mitoses in the parietal cells in man were recognized by Böhm-Davidoff (1895), Nauwerk (1897), Popoff (1897), Ascoli (1901), Lim (1922), Zimmermann (1925) and Plenk (1931). Tortora (1899), Cade (1900, 1901), Malesani (1909), Kirk (1910), Harms (1910), and Debernardi (1912) also described the above mentioned cell-divisions in animals. On the other hand, however, Harvey (1907) and Ulkan (1912) denied the mitoses in the same cells. Ohishi (1947) said that the parietal cells proliferated mainly through the amitoses in man, and Sunohara (1955) has reached the similar conclusion in man and rat. The mitoses in these cells were rarely recognized by Ohishi, but Sunohara did not observe such division. Bizzozzero (1893), Salomon (1893), Bensley (1898), Cade (1901), Liebert (1904), Harvey (1907), Lim (1922), Zimmermann (1925), Ohishi (1947) and Sunohara (1955) denied the mitoses in the chief cells and they, including Maximow-Bloom (1958) and Tokari (1960), excepting Sunohara, considered that the same cells were able to originate in the mucous neck cells. Kida (1938), however, denied this opinion. Ohishi said that she recognized the transformation between the mucous neck cells and the chief cells, but could not affirm the transforming direction in them. According to the results basing upon the isolated preparations, Sunohara described that the division in the chief cells were due to the amitoses and Ohishi rarely recognized the same cell-divisions in the sections. While, Salvioli

(1890), Bizzozzero (1893), Böhm-Davidoff (1895), Malesani (1909), Kirk (1910) and Harms (1910) described the mitoses in the chief cells, but all of their opinions, except Kirk's, have not been believed because of their misjudgments on their researches. Some investigators, such as Bensley (1898), Cade (1901), Liebert (1904), Harvey (1907), Lim (1922), Zimmermann (1925), Sunohara (1955), Stöhr (1959) recognized the mitoses in the mucous neck cells. Ohishi (1947) and Tokari (1960) said that mitoses in the same cells were rarely found, and the former considered that those cells proliferated mainly through the amitoses. Ishizawa (1951), Maximow-Bloom (1958) and Bloom-Fawcett (1962) denied the mitoses in the above mentioned cells and they, including Tokari, considered that the new mucous neck cells were probably able to arise through a gradual transformation of the undifferentiated epithelium in the bottom of the foveolae and in the neck regions of the glands. Sachs (1887), Meyer (1889), Ewald (1893), Boas (1894), Hayem (1894), Schmidt (1895), Popoff (1897), Lubarsch (1897), Leuk (1899), Letulle (1900), Einhorn (1902), Boeckelmann (1902), Harvey (1907), Heyrowsky (1913), Stoerck (1922), Paschkis-Orator (1923), Oshikawa (1923), Borst (1923), Moszkowicz (1924), Lauche (1924), Konjetzny (1928), Lehner (1928), Hamperl (1928) and Ishizawa (1951) described that it was possible that the mucous neck cells might arise through a transformation of the chief cells. We, the present authors, denied this opinion, basing upon their data of the histochemical investigations on the fundic glands in the Japanese monkeys (1965). After that, they have made a thorough investigations on the cell-divisions in the parietal, chief and mucous neck cells to affirm the origin and the replenishment of those cells and they will inform on the result in this report.

Materials and Methods

Two puppies, aged one month and three months, four adult dogs, four Japanese monkey (*Macaca fuscata yakui*) and seven human stomachs were used for the present study. The animals were killed by a rapid intravenous injection of Nembutal, and the human materials were obtained from the normal part of the resected cancerous or ulcerous stomachs. The materials were taken in as fresh a state as possible from the fundus, lesser and greater curvature regions. The tissues were fixed in buffered formalin, embedded in paraffin and

cut in $4-6\mu$ thin sections. The sections were stained with hematoxylin (Harris)-eosin, Heidenhain's iron hematoxylin, PAS reaction and 41×10^{-4} toluidine blue solution. The nuclei in the mitoses are stained dark blue or greenish blue by the last described solution, due to the increase of quantity of DNA. While the resting nuclei are lightly stained. So, it is convenient to find the mitoses in the section preparations. The above described color characteristics in the mitoses cannot be recognized in the amitoses. We have made a thorough investigation in the presence of the mitoses and amitoses in the parietal, chief and mucous neck cells, but have not treated statistically.

Observations

1. Parietal cells (Figs. 1-6)

The mitoses in the parietal cells are rarely found in the adult dogs, monkeys and men. But they are not so rare in the one-month- and three-month-old puppies. The amitoses in the same cells are generally observed in the above described materials. As the nuclear divisions in the parietal cells are not always followed by the division of the cell bodies, we can recognize many polynuclear parietal cells in the section preparations. We do not meet a form of dumb-bell in the nucleus or cell body in the processes of the amitoses, and two daughter nuclei are connected with slender caryoplasm. There is a straight division line between two daughter cells but such a line is not observed in the cell whose daughter nuclei keep too close. The division in the cell body begins in one side and reaches the other. This division line is PAS-positive, so we can clearly recognize the process of division in the section preparation.

2. Chief cells (Figs. 7-10)

The mitoses in the chief cells are frequently observed in the one-month-old puppy, while they are fewer in the three-month-old puppy as well as in the adult dogs, monkeys and men. And yet we have not difficulty in finding them out. Namely, we observed such cell divisions in each three out of the four dogs and the four monkeys and two out of the seven men. It is to be noted especially that we could find the mitoses in the stomachs of the two Japanese monkeys which were filled up with feed, and that we could also recognize a few mitoses in one out of the two monkeys which were killed about thirty seven hours after meal. Although, we often recognize the mitoses in the so-called immature chief cells (Figs. 11, 12, 15), we can

find them sometimes also in the chief cells in the bottom of the glandular tubules. The so-called immature chief cells are distributed in the body parts of the glands and we consider that they are the remains in the processes of embryogenesis and they also originate in the mucous neck cells. Regarding this fact, we will inform in another report. By the way, many two-nuclear chief cells were found in any section with or without mitoses regardlessly.

3. Mucous neck cells (Figs. 11, 13-16)

We can easily find the mitoses in the mucous neck cells in the adult dogs, monkeys and men, even if the same cell-divisions are not observed in the chief cells in the same sections.

Discussion

Parietal cells

Böhm-Davidoff (1895), Nauwerk (1897), Popoff (1897), Ascoli (1901), Lim (1922), Zimmermann (1925) and Plenk (1931) recognized the mitoses in the parietal cells in man. Tortora (1899), Cade (1900, 1901), Malesani (1909), Kirk (1910), Harms (1910) and Debernardi (1912) described the same cell-divisions in animals. While, Harvey (1907) and Ulkan (1912) denied it. Ohishi (1947) considered that the cell-divisions in the parietal cells in man mainly arised through the amitoses, and Sunohara also maintained similar opinion in man and rat. According to the researches on the dog, Japanese monkey and man, we, the present authors, approved of the opinions of Ohishi and Sunohara. We have difficulty in finding out the mitoses in the same cells even in the one-month-old puppy, while the same cell-divisions are easily observed in the chief cells in the same sections. Sunohara could not find the mitoses in the parietal cells in man and rat, while, be rare as it may, we found those in the dog, Japanese monkey and man, and Ohishi also recognized similar division in man. We frequently found the nuclear divisions in the parietal cells but these divisions did not always follow those of the cell bodies. So we very often meet with the polynuclear cells in the same cells. The multiplication of those cells depends on the above mentioned cell-division, moreover, they are supplied from the undifferentiated cells which are distributed in the neck region of the glands. On this fact, we will make a detailed explanation in the following report.

Chief cells

Salvioli (1890), Bizozero (1893), Böhm-Davidoff (1895), Malesani (1909), Kirk (1910) and Harms (1910) described the mitoses in the chief cells, but excepting Kirk's opinion, the others' are not believed for their misjudgment on the difference between the mucous neck cells and the chief cells. On the other hand, Bizozero (1893), Salomon (1893), Bensley (1898), Cade (1901), Liebert (1904), Harvey (1907), Lim (1922), Zimmermann (1925), Ohishi (1947) and Sunohara (1955) denied that division type. Moreover, they, including Maximow-Bloom (1958) and Tokari (1960), excepting Sunohara, consider that those cells can possibly arise through the transformation of the mucous neck cells, but this opinion was denied by Kida (1938). Ohishi recognized the transformation between the mucous neck cells and the chief cells, but she said that it was impossible to affirm the transforming directions in them. Sunohara maintained that the divisions in the chief cells arise through the amitoses. We, the present authors, frequently observed the mitoses in the chief cells in the one-month-old puppy, and they didn't have difficulty in finding out the same cell-divisions in the three-month-old puppy, adult dogs, Japanese monkeys and men, especially in their immature chief cells. Namely, we recognized considerable mitoses in each three out of the four adult dogs and two out of the seven men. But basing upon the fact that there are many two-nuclear chief cells in the section preparations, and upon the result of Sunohara which was made on the isolated preparations, we consider that those cells can divide into high frequency through the amitoses, and on this occasion, the amitotic proliferations in the chief cells seem to be principal. It is true that we cannot observe any mitotic division in the chief cells in some dogs, Japanese monkeys and men, but we interpret that the materials or sections we investigated happened to be those of nondividing period. After all, we obtained the undeniable fact that there were some more or less mitoses in the chief cells in man and animal.

In addition to the above mentioned cell multiplication, the chief cells are supplied from the immature chief cells which are the remains in the processes of embryogenesis and they also arise from the mucous neck cells and transform into the chief cells. We will report on this fact in detail on another opportunity (Report II).

Mucous neck cells

Bensley (1898), Cade (1901), Liebert (1904), Harvey (1907), Lim (1922), Zimmermann (1925), Sunohara (1955) and Stöhr (1959) recognized the mitoses in the mucous neck cells. Sunohara found out only the same cell-divisions in man and rat, and could not find the amitoses in those cells in the isolated preparations. Ohishi (1947) rarely recognized such cell-divisions and emphasised that the proliferation of those cells depended on the amitoses. Ishizawa (1951), Maximow-Bloom (1958) and Bloom-Fawcett (1962) denied the mitoses in those cells, and they, including Tokari (1960), considered that the new mucous neck cells were probably able to arise through a gradual transformation of the undifferentiated epithelium in the bottom of the foveolae and in the neck region of the glands. Miyake and Kaku (1963) found out the generation zone in the neck region of the glands by means of ^3H -thymidine radioautograph and they recognized that the generative cells were able to transform into the mucous neck cells. On the other hand, Sachs (1887), Meyer (1889), Ewald (1893), Boas (1894), Hayem (1894), Schmidt (1895), Popoff (1897), Lubarsch (1897), Leuk (1899), Letulle (1900), Einhorn (1902), Boeckelmann (1902), Harvey (1907), Heyrowsky (1913), Stoerck (1922), Paschkis-Orator (1923), Oshikawa (1923), Borst (1923), Moszkowicz (1924), Lauche (1924), Konjetzny (1928), Lehner (1928), Hamperl (1928), Ohishi (1947) and Ishizawa (1951) considered that the mucous neck cells might arise through a transformation of the chief cells.* We, the present authors, frequently found out the mitoses in the mucous neck cells in the adult dogs, Japanese monkeys and men, even the above mentioned divisions were not recognized or were very rare in the chief cells in the same section preparation. We have no firm foundation for denying the amitoses in the mucous neck cells, but basing upon our result and Sunohara's research, we also consider that the proliferation in those cells are mainly dependent upon the mitoses. Ladman (cite from Bloom-Fawcett, 1962) considers by means of ^3H -thymidine radioautograph that the principal site of mitoses exists in the neck regions of the gastric glands. And then we deny the above mentioned opinion* on the foundation of their present research and the histochemical differences between the mucous neck cells and the chief cells which will be subsequently reported. Moreover, the mucous neck cells arises from the undifferentiated cells which are mixed in them.

Summary

After the observations on the cell-divisions in the gastric glands in two puppies, each four adult dogs and Japanese monkeys and seven men, the authors have obtained the following results.

1. The parietal cells proliferate mainly through the amitoses, moreover, be rare as it may, we can also find out the mitoses.

2. It is true that the amitoses take the lead in the proliferation in the chief cells and that most of the investigators deny the mitoses in those cells, but we have no difficulty in finding out the mitoses in the same cells in the adult dogs, Japanese monkeys and men.

3. The proliferations of the mucous neck cells are dependent upon the mitoses in the cells of the same kind, and the present authors deny the opinion which maintain the arising of those cells through a transformation of the chief cells.

4. The parietal, chief and mucous neck cells are also replenished by the transformation of the undifferentiated cells in the neck region of the glands. We will inform those facts in detail in other reports.

Acknowledgement

The authors heartily appreciate the kindness of Dr. Y. Iyomasa, School of Medicine, Nagoya University, who offered to us the human stomachs.

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Plate I.

Explanation of figures

- Fig. 1. Mitosis in the parietal cell (↑) in man, stained with 41×10^{-4} toluidine blue solution. $\times 1,000$
- Fig. 2. Mitosis in the parietal cell (↑) in the Japanese monkey, stained with 0.05% toluidine blue solution at pH 2.5. $\times 1,000$.
- Fig. 3. Mitosis in the parietal cell (↑) in the dog, stained with hematoxylin-eosin. $\times 550$.
- Fig. 4. Amitosis in the parietal cell (↑) in man, but cytoplasmic division does not arise yet. Periodic acid-Schiff-hematoxylin. $\times 1,000$.
- Fig. 5. Amitosis in the parietal cell in man. PAS-positive dividing line in the cytoplasm is partly seen (↑). Periodic acid-Schiff-hematoxylin. $\times 1,000$.
- Fig. 6. Trinucleate parietal cell (↑) in man. Dividing line in the cytoplasm is not seen. Periodic acid-Schiff-hematoxylin. $\times 1,000$.
- Fig. 7. Mitosis in the chief cell (↑) in man, stained with hematoxylin-eosin. $\times 550$.
- Fig. 8. Mitosis in the chief cell (↑) in the Japanese monkey, stained with 25×10^{-4} toluidine blue solution. $\times 1,000$.

Plate II.

Explanation of figures

- Fig. 9. Mitosis in the chief cell (↑) in the dog, stained with 1% cresyl violet. $\times 1,000$.
- Fig. 10. Mitosis in the chief cell (↑) in the dog, stained with hematoxylin-eosin. $\times 550$.
- Fig. 11. Mitosis in the mucous neck cell (1) and the immature chief cell (2), and the chief cell (3) in the Japanese monkey, stained with 0.05% toluidine blue solution at pH2.5. $\times 330$.
- Fig. 12. Mitosis in the immature chief cell (↑) in the dog, stained with 1% cresyl violet. $\times 1,000$.
- Fig. 13. Mitosis in the mucous neck cell (↑) in man, stained with 0.05% toluidine blue solution at pH2.5. $\times 550$.
- Fig. 14. Mitosis in the mucous neck cell (↑) in the Japanese monkey, stained with 0.05% toluidine blue solution at pH2.5. $\times 550$.
- Fig. 15. Mitosis in the mucous neck cell (1) and the immature chief cell (2) in the dog, stained with 0.05% toluidine blue solution at pH4.1. $\times 1,000$.
- Fig. 16. Mitosis in the mucous neck cell (↑) in the dog, stained with hematoxylin-eosin. $\times 550$.

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