Do the Cardiac Glands Exist?

5. The dog

By

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Summary: The authors performed histological and histochemical investigations on the so-called cardiac glands and gastric glands of the dog, and compared the data on these glands. The conclusions were as follows:

1. The so-called cardiac glands have a number of parietal cells and cells distributed in the same glandular base contain fine pepsinogen granules. However, these glandular cells are filled with a PAS-positive substance. Accordingly, the so-called cardiac glands are nothing but undifferentiated gastric glands.

2. Due to the deep gastric pits, the outer layer of the mucous membrane in the clear zone is loose, and a distribution of a smaller number of blood vessels can be expected. These facts may demonstrate a pale or clear appearance of the mucous membrane in the same zone.

3. The gastric pits in the dark zone are extremely shallow. Accordingly, the mucous membrane in this area is dense and a distribution of a large number of blood vessels can be expected. This probably produces a dark color, i.e., reddish brown.

4. The chief cells in the glandular base of the clear zone contain a number of fine and coarse PAS-positive granules. These granules also are a violet color with PAS-AB (pH 2.5) stain. This color resulted from sialomucin. The above mentioned facts mean that the clear zone is an undifferentiated region of the gastric glands.

5. The chief cells distributed in the glandular body and base of the dark zone are PAS-negative and contain no sialomucin. Accordingly, the same zone is the differentiated region of the gastric glands.

6. The chief cells of the gastric glands in the cardiac region and clear zone contain a small quantity of weak and strong acid mucopolysaccharides, while those cells in the dark zone surpass the above-mentioned cells in the quantity of the same substances.

7. The weak and strong acid mucopolysaccharides were also recognized in the mature chief cells of the cat. However, we could not find any in man, macaque or many other types of animals studied.

The glands distributed in the narrow region neighboring the end of the dog esophagus have been described as the cardiac glands^{1,7-10}. Imai *et al.* investigated these glands in the macaque², swine³, humans⁴ and horse⁵ and demonstrated that these

glands were nothing but undifferentiated gastric glands. This paper provides a detailed description of the same glands of the dog.

The textbooks on the anatomy of domestic animals^{1,7,9,10} describe the gastric mucous membrane as being divided into two zones

Fig. A. Diagram of zones in the mucous membrane of dog stomach (after Nickel *et al.*)

- 1 : Esophagus
 - 2 : Cardiac gland
 - 3' : Clear zone
 - 3'' : Dark zone
 - 4 : Pyloric gland zone
 - 5 : Duodenum
- } Gastric gland zone

except the cardiac and pyloric gland regions of the dog. The one on the esophageal side is the clear zone and the other on the pyloric side is the dark zone (Fig. A). However, no effort has been made to resolve the substance of these zones. The authors have performed detailed histological and histochemical observations on these regions and demonstrated their contents.

Materials and Methods

Seven adult dog stomachs were used. Three were used for the so-called cardiac glands and seven stomachs were for the clear and dark zones. The dogs were killed by a rapid intravenous injection of about 1.5-2.0cc Nembutal. Samples were taken in as fresh a state as possible from the cardiac region in-

cluding the end of the esophagus, clear and dark zones, and fixed in buffered formalin. The tissues were embedded in paraffin and cut into sections of about 6μ in thickness. The staining techniques were as follows. For the so-called cardiac glands: PAS-, AB (pH 2.5 and 0.5) stains and Bowie's method for pepsinogen granules. For the clear and dark zones: PAS-, Zimmermann-, AB (pH 2.5 and 0.5)-, PAS-AB (pH 2.5) stains and Bowie's method for pepsinogen granules.

Observations

I. The so-called cardiac glands

These were distributed in the narrow area neighboring the esophageal orifice. They were simple tubular glands and a few of them next to the esophagus were fairly short (Figs. 1, 2). A number of parietal cells were found in the same glands (Fig. 3). Receding from the esophagus, these cells increased in number.

1. PAS stain: The glandular cells reacted strongly to PAS (Figs. 1-3).

2. AB (pH 2.5 and 0.5) stains: The glandular cells reacted negatively or very weakly to the same stains (Figs. 4, 5).

3. Bowie's method for pepsinogen granules: A fairly large number of fine granules were found in the cells of the glandular base (Fig. 6).

II. The clear zone

The gastric pits in this area were deep and occupied about half the thickness of the mucous membrane. Accordingly, the gastric glands were short. Due to these facts, the structure of the outer layer of the mucous membrane in this zone was very loose (Fig. 7).

The mature chief cell layer in the clear zone was thin.

1. PAS and Zimmermann stains: The mucous neck cells and immature chief cells

reacted strongly to PAS and a small quantity of PAS positive substance remained in the mature chief cells (Fig. 7). Occasionally, the immature chief cells were found among the mature chief cells in the glandular base (Fig. 7). The immature chief cells were usually distributed in the glandular body. The immature chief cell layer was slightly thicker than that of the mature chief cells. The parietal cells were found among the immature chief cells and there were fewer than the immature cells.

2. AB (pH 2.5 and 0.5) stains: The mature chief cells reacted negatively or weakly to the same stains (Figs. 9, 11).

3. PAS-AB (pH 2.5) stain: The epithelium of the mucous membrane and gastric pits were dark blue. Sometimes the latter assumed a dark blue or mixed deep red color. The mucous neck cells were violet and the immature chief cells were deep red. The mature chief cells reacted weakly to AB and contained a large number of violet fine granules (Fig. 13).

4. Bowie's method for pepsinogen granules: The chief cells in the glandular base contained a number of light blue and fairly fine pepsinogen granules. The same granules in the PAS-positive cells were fine and claret colored (Fig. 15).

III. The dark zone

The gastric pits in this area were very shallow (about $1/4 \sim 1/5$ the thickness of the mucous membrane). Accordingly, the structure of the membrane in the same zone was dense. The glands occupied a great portion of the mucous membrane. The chief cells in the middle and lower portions of the body and base of the glands completed their differentiation (Fig. 8). A large number of the parietal cells were distributed among the chief cells, especially in the immature chief cell layer and surpassed the same cells in number.

1. PAS and Zimmermann stains: The mucous neck cells and immature chief cells in

the upper part of the glands reacted strongly to PAS. The PAS positive substance was unrecognizable in the mature chief cell (Fig. 8).

2. AB (pH 2.5 and 0.5) stains: The mature chief cells reacted weakly or moderately to the same stains (Figs. 10, 12).

3. PAS-AB (pH 2.5) stain: The mucous neck cells were violet, immature chief cells were deep red and mature chief cells reacted weakly to AB and violet granules such as those in the chief cells of the clear zone were not observed (Fig. 14).

4. Bowie's method for pepsinogen granules: The mature chief cells contained a large number of dark blue coarse pepsinogen granules (Fig. 16).

Discussion

I. Do the cardiac glands exist?

The authors observed the so-called cardiac gland area and confirmed that these simple tubular glands had a number of parietal cells, and found a fairly large number of fine pepsinogen granules in the glandular cells of the basal part of the glands. These cells were filled with a PAS-positive substance. Namely, they were undifferentiated chief cells. We consider, therefore, that the cardiac glands are nothing but undifferentiated gastric glands. Consequently, the cardiac glands do not exist in the dog stomach.

II. The substance of the clear and dark zones in the mucous membrane.

The authors performed detailed histological investigations on the clear and dark zones and found the following structural differences between both zones.

1. The gastric pits in the clear zone are deep and occupy about half the thickness of the mucous membrane. Accordingly, the structure of the outer layer of the same membrane is

loose and such a structure may result in a small distribution of blood vessels in that layer. For this reason, it is possible to show a pale or clear appearance of the same zone.

2. The gastric pits in the dark zone are very shallow and occupy about $1/4 \sim 1/5$ the thickness of the mucous membrane. Accordingly, the structure of the same membrane is dense, and a distribution of a large number of blood vessels can be expected. The above-mentioned facts probably produce a dark color, i.e., reddish brown. As a result, the authors consider that the depth of the gastric pits is an important factor in producing the color of the mucous membrane in the clear and dark zones.

III. The characteristics of the gastric glands in the clear and dark zones.

1. The gastric glands in the clear zone: They are short and the strongly PAS-positive immature chief cell layer occupies the glandular body, and it is thicker than the mature chief cell layer in the glandular base. Sometimes, the former layer spreads into the latter layer. The mature chief cells contain a number of fine and coarse strongly PAS-positive granules. This means these cells are still in an immature or undifferentiated stage. The same granules also are a violet color by PAS-AB (pH 2.5) stain. This color indicates the existence of sialomucin in the above-mentioned cells.

2. The gastric glands in the dark zone: They are longer than those in the clear zone, and the PAS-positive immature chief cell layer is very thin. On the contrary, the PAS-negative chief cell layer is extremely thick. Namely, the mature chief cells are distributed not only in the glandular base but also in the greater part of the glandular body. The mature chief cells in the body are somewhat smaller than those in the base. The pepsinogen granules in the mature chief cells are coarse and dark blue. It can be concluded from the above that the

clear zone is an undifferentiated zone of the gastric glands, and the dark zone is a differentiated zone of the same glands. The reactions to the weak and strong acid mucopolysaccharides in the chief cells of the gastric glands neighboring the esophagus and mature chief cells in the clear zone are weak. On the other hand, the mature chief cells in the same glands of the dark zone are moderate. The above-mentioned reactions in the mature chief cells of the cat gastric glands are fairly strong⁶⁾. These mucopolysaccharides in the mature chief cells of the cat and dog are unrecognizable in the same cells of the Japanese macaque²⁾, crab-eating monkey²⁾, swine³⁾, humans⁴⁾, horse⁵⁾, cow, rabbit, mouse and rat (unpublished).

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Explanation of Figures

(All related to dog)

Plate I

Fig. 1. Terminal part of the esophagus and cardiac glands. PAS stain. $\times 23$.

↑ : Esophagogastric junction.

A : Cardiac glands react strongly to PAS.

B : Esophageal stratified squamous epithelium.

C : Esophageal glands. A number of the same glands extend into the cardiac region (D).

Fig. 2. Cardiac glands neighboring esophagogastric junction. PAS stain. $\times 115$.

A : Esophageal stratified squamous epithelium.

Fig. 3. Enlarged photo of the same portion in Fig. 2. PAS stain. $\times 230$.

A number of parietal cells (↑) are distributed in the cardiac glands.

A : Esophageal stratified squamous epithelium.

Fig. 4. Cardiac glands (↑) react negatively or very weakly to AB (pH 2.5). AB (pH 2.5) stain. $\times 115$.

A : Esophageal stratified squamous epithelium.

Fig. 5. Cardiac glands (↑) reaction negatively or very weakly to AB (pH 0.5). AB (pH 0.5) stain. $\times 115$.

A : Esophageal stratified squamous epithelium.

Fig. 6. Pepsinogen granules in the cardiac gland. Bowie's method for pepsinogen granules. $\times 57.5$.

Some fine granules (↑) are recognizable in the glandular cells.

Fig. 7. Gastric glands in the clear zone. Gastric pits are deep. Zimmermann stain. $\times 57.5$.

A : Mucous neck cells.

B : Immature chief cells in the glandular body.

C : Mature chief cells in the glandular base.

Fig. 8. Gastric glands in the dark zone. Gastric pits are shallow. Zimmermann stain. $\times 57.5$.

A : Mucous neck cells.

B : Immature chief cells in the upper portion of the glandular body.

C : Mature chief cells in the middle and lower portions of the glandular body.

D : Mature chief cells in the glandular base.

Plate II

- Fig. 9. Gastric glands in the clear zone. Mature chief cells (A) react negatively or weakly to AB (pH 2.5). AB (pH 2.5) stain. $\times 115$.
- Fig. 10. Gastric glands in the dark zone. Mature chief cells (A) react weakly or moderately to AB (pH 2.5). AB (pH 2.5) stain. $\times 115$.
- Fig. 11. Gastric glands in the clear zone. Mature chief cells (A) react negatively or weakly to AB (pH 0.5). AB (pH 0.5) stain. $\times 115$.
- Fig. 12. Gastric glands in the dark zone. Mature chief cells (A) react weakly or moderately to AB (pH 0.5). AB (pH 0.5) stain. $\times 115$.
- Fig. 13. Gastric glands in the clear zone. PAS-AB (pH 2.5) stain. $\times 57.5$.
A : Immature chief cells in the glandular body assume a deep red color.
B : Mature chief cells contain a number of fine and coarse violet granules. The cytoplasm of the same cells react weakly to AB (pH 2.5). However, the above-mentioned facts are indistinguishable in this picture.
- Fig. 14. Gastric glands in the dark zone. PAS-AB (pH 2.5) stain. $\times 57.5$.
A : Immature chief cells assume a deep red color.
B : Mature chief cells react weakly to AB (pH 2.5).
- Fig. 15. Pepsinogen granules ($\uparrow$) in incompletely differentiated mature chief cells of the clear zone. These granules are fairly fine and claret-colored. Bowie's method for pepsinogen granules. $\times 575$.
- Fig. 16. Pepsinogen granules in mature chief cells of the dark zone. These granules are coarse and dark blue. Bowie's method for pepsinogen granules. $\times 575$.