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HISTOLIOGIC CHANGES OF THE ANTERIOR HYPOPHYSIS IN SANDMEYER DOGS

by

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(Received for publication Oct. 5, 1959)

INTRODUCTION

Since the glycosuria caused by the extirpation of the pancreas was demonstrated by MERING & MINKOWSKI (1889) in dogs, RENAZI & REALE, PFLÜGER, ALLEN, and others accomplished many valuable studies on experimental diabetes produced by partial pancreatectomy. SANDMEYER devoted himself particularly to permant diabetes caused by the extirpation of the greater part of the pancreas. Hence, PFLÜGER designated this type of diabetes as "Sandmeyer diabetes", although SANDMEYER was by no means the first to describe about the diabetes of such a type. When ROCKEY (1943) performed the total pancreatectomy in men for the first time, he administered a great amount of insulin to combat for severe diabetes mellitus, and encountered severe and prolonged insulin shock. Later, he found that in diabetes produced by total pancreatectomy, the insulin requirement hardly exceeded 27 units daily on average, which amount was far less than could be anticipated from the experiences of treating patients suffering from diabetes mellitus.

In the same year, DRAGSTEDT pointed out that compared with the totally pancreatectomized dogs, the diabetic dogs with a small pancreatic remnant required far greater amount of insulin, and mentioned that in deabetic dogs with a small pancreatic remnant, digestion and absorption were somewhat better compared with the totally pancreatectomized dogs, and this fact may be considered to be a factor for their greater insulin tolerance, but this alone cannot constitute a sufficient explanation.

With regard to these apparently contradicted findings, it can naturally be considered that multiple factors related to the endocrinic organs may be involved.

In 1930, HOUSSAY et al. reported that the diabetic state of the totally pancreatectomized dogs was alleviated by the extirpation of the hypophysis. On the other hand, YOUNG could produce permanent diabetes by continued administration of the extract of the anterior hypophysis. These findings suggest that the anterior hypophysis plays an important role in connection with the character of the diabetes produced by pancreatectomy.

In his study on the distribution of the anterior pituitary cells in totally pancreatectomized dogs, HASEGAWA made it clear that the chromophil cells exhibited a

marked tendency of decrease, and discussed that this fact indicated a spontaneous occurrence of HOUSSAY's phenomenon.

In the present study, as a means of ascertaining the difference in the insulin requirement between totally pancreatectomized dogs and Sandmeyer dogs, an investigation was qualitatively and quantitatively made on histological changes in the anterior hypophysis of Sandmeyer dogs.

MATERIAL AND METHOD

Adult mongrel dogs were used as test animals, excluding those in pregnancy or lactation. All the test animals were subjected to the determination of the blood sugar level and to the test of urinary sugar prior to operation, so as to ascertain that they were not diabetic. After the operation, their blood sugar level at the time of empty stomach was recorded every week.

After permanent diabetes had been produced, crystalline insulin was intramuscularly injected before each meal. In order to determine the required dose of insulin, the urine specimen was examined 3～5 hours after meal and according to the content of urine sugar, the amount of insulin to be prescribed was regulated so that urine sugar would maintain a level of 0～0.25 per cent. If required, the daily amount of urine and that of urine sugar were determined, and 0.2 units of regular insulin per kg in body weight were injected intravenously, and changes in the blood sugar level were observed.

The determination of urine sugar was carried out by ELI LILLY'S "TES-TAPE" and that of the blood sugar level by HAGEDRON-JENSEN method.

According to PFLÜGER, the pancreas of dogs can be divided into three portions, namely, the processus uncinatus, corpus, and processus lienalis, and these portions correspond to the head, body and tail of the human pancreas respectively. In dogs, the pancreas and the duodenum very freely movable, and easily accessible compared with these organs in men.

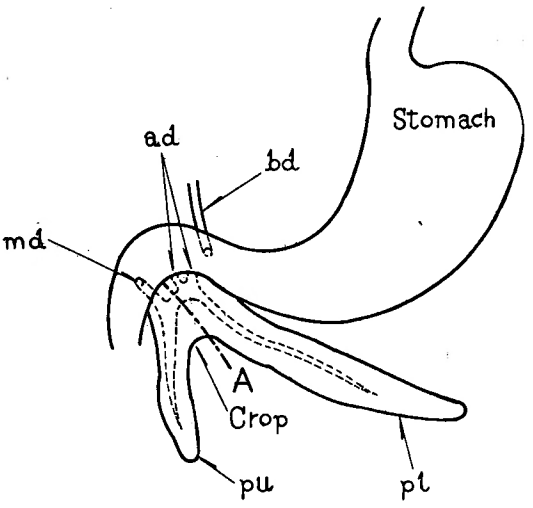
After fasting for one day, test animals were subjected to the operation. An upper mid-line incision was employed, and the main pancreatic duct was found at the part where the pancreas and the duodenum are most compactly connected with each other. When this duct was searched out, the body of the pancreas was separated from the duodenum at the point 5～7 mm distant from the duct on the splenic process side with ample care so as not to injure the pancreato-duodenal vessels, and then as shown in Fig. 1, after double ligations encircling the pancreas, the body of the pancreas was cut through, and thus about two thirds of the body of the pancreas was removed together with the processus lienalis en masse.

Next, the uncinate process was to be extirpated. This could, however, be performed with comparative ease. After that, about one third of the body of the pancreas with the main pancreatic duct at its top end was left, and the consideration for the main pancreatic duct in the second operation and onwards could be very much mitigated. So long as the dissection was correct, the common bile duct was left intact. The coverning over the operation field with the omentum, prevented

the pancreas from having adhesions to the liver, facilitating the procedure of the next operation. After the operation, glycosuria might transiently be observed, but it disappeared almost within one week.

The second operation was carried out 1~2 months after the first operation. In this time, the main pancreatic duct had been located at the top edge on the splenic process side of the pancreatic remnant as mentioned above. Accordingly, by performing partial pancreatectomy from the side of the uncinate process, the remnant of the desired size could be left around the main duct. In most cases, although the pancreas was in a sclerotic atrophic state, it was not difficult to remove with ligature en masse. After the second operation, permanent diabetes would occur in most cases directly after the operation or sometimes 1~2 weeks later. In case the produced diabetes was found still to be transient, the third partial pancreatectomy should have been added.

Fig. 1



md : main duct of pancreas
ad : accessory ducts of pancreas
bd : bile-duct
corp : corpus pancreatis
pu : processus uncinatus
pl : processus lienalis
A : cut-Line

HISTOLOGICAL EXAMINATION OF THE ANTERIOR PITUITARY LOBE

The pituitary gland was extirpated by craniotomy directly after test animals were sacrificed, and was fixed for 24 hours with BOUIN's fluid diluted to twice its volume, and then, was divided into two parts, that is, the upper and lower parts by the intermediate horizontal section, and they were embedded in paraffin respectively. From their horizontal sections, horizontal serial sections of three microns thick were obtained, being subjected to the haematoxylin-eosin stain, Kresazan stain, and PAS-azan stain. The glandular cells of various types were qualitatively and quantitatively examined. The calculation of each type of glandular cells was made by RASMUSSEN-HERRICK'S method modified by INOUYE.

RESTLTS OF EXPERIMENT

A. Control group

Normal dogs were used as control. From the results of morphological chromatological investigations on the granules in the cytoplasma, referring to the shape and size of the cytoplasmas and nuclei, I could classify the glandular cells into 5 types as follows.

1) The first type cells:

The cells were not so large in size. They had fine granules stained extremely thick red in their cytoplasma. The nuclei proved to be very polymorphous in every cell. However, the nuclei belonging to this type were generally small, and many were found to be rich in chromatin.

2) The second type cells:

They were similar to the aforementioned cells, but the granules were rough and reddish, but a yellowish tone prevailed. This type was rather difficult to discriminate from the cells mentioned above unless the staining technique was properly done.

3) The third type cells:

Compared with other cells, they were distinctly large, having rough granules stained bluish violet on red purple. The nuclei were generally large in size, and many of them were noted to have lightly been stained.

4) The forth type cells:

This type of cells resembled to the cells of the third type, but they were somewhat smaller in size. The granules were relatively small and dominated with a bluish tone. The many nuclei were found to be resembling to those cells of the first type.

5) The fifth type cells:

In this type, the protoplasma was indistinct. The granules assumed a slight purplish tone, but it was so faint that they might easily be taken to be the nuclei alone at the first glance.

The above-mentioned cells are the α-, ε-, β-, δ-, and γ-cells of ROMEIS respectively. In the meantime, GOLDBERG and CHAIKOFF advocated the presence of the ζ-cells in male dogs.

However, opinions split as to whether various appearances of these cells are the representation that they belong to different systems respectively, or the manifestation of various phases of the cells beloging to a single or several systems. Therefore, with a view to excluding any error in the case of any transitional type, they were classified into the following three types:

I-type cells, (the α-cells and the ε-cells)

II-type cells, (the β-cells and the δ-cells)

III-type cells, (the γ-cells)

Table 1 Distribution of the Anterior Pituitary Cells in Normal Dogs.

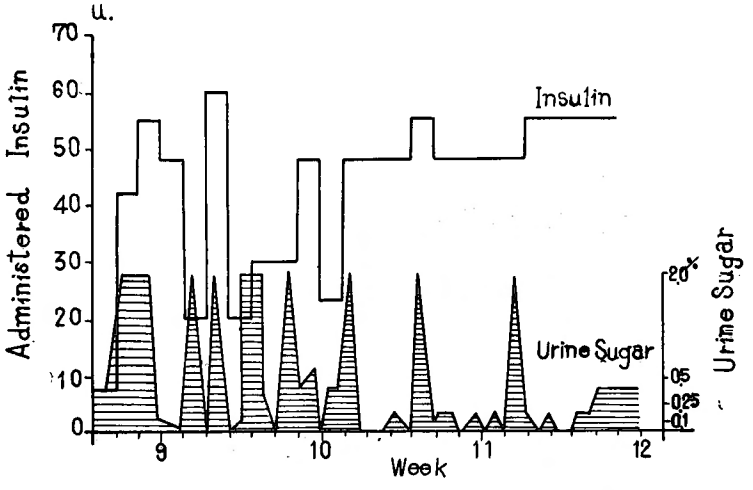
Dog Number	Sex	Body weight kg	Pituitary weight mg	Percentage of cell types		
				Type I	Type II	Type III
1	Male	12.3	80	44.6	6.1	49.3
4	〃	10.8	50	43.8	4.8	51.4
30	〃	12.3	60	46.1	7.8	46.1
32	〃	8.8	70	46.4	5.3	48.3
37	Female	9.6	70	42.6	6.2	51.2
	Mean			44.7 ± 0.71	6.0±0.51	49.3 ± 0.98

The distribution of the glandular cells by the above-mentioned classification of the anterior pituitary lobe in normal dogs is as given in Table 1. The mean value of the 5 cases were 44.7% (± 0.71) for the I type, 6.0% (± 0.51) for the II type and 49.3% (± 0.98) for the III type respectively.

B. Sandmeyer Dogs

In the dogs in which severe permanent diabetes was produced by partial pancreatectomy, the disturbance of the regulation of the blood sugar level was seen 2～3 weeks after the start of the insulin administration. In this period, the hypoglycemic symptoms caused by insulin were often encountered. The dose of insulin administered showed heavy shiftings on and off with a tendency to increase with the lapse of time. Fig. 2 gives the relationship between the level of urine sugar and the dose of insulin in a typical example of Sandmeyer dog.

Fig. 2 Amount of Insulin administered and that of Urine Sugar in Typical Sandmeyer Dog.

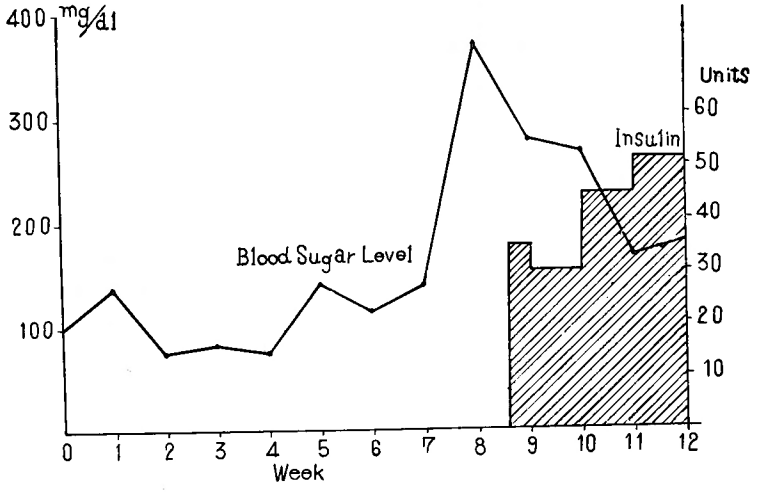


Then, was established a state wherein the regulating mechanism of the blood sugar level had been balanced, and although there were differences in the doses of insulin as shown in table 2 depending upon the cases, the urine sugar content was found low after the meal, as long as an adequate amount of insulin was administered, while the blood sugar level at the time of empty stomach was approximately

Table 2 Amount of Insulin administered in Sandmeyer Dogs.

Dog No.	Since occurence of Diabetes. weeks	Units/day
10	10	50
21	5	53
22	5	52
23	9	40
24	6	40
26	9	70
28	4	72
29	3	36
31	5	55

Fig. 3 Changes of the Blood Sugar Level and of the Amount of Insulin administered in Typical Sandmeyer Dog (No. 22).

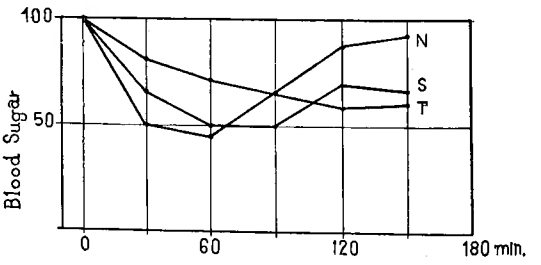


stabilized within the range of 100～200 mg/dl.

Fig. 3 gives a typical example showing the relation between the blood sugar level at the time of empty stomach in Monday morning every week, and the mean of daily doses of insulin during the week. These animals indicated a tendency to increase in their body weight (refer to Table 3), and also showed greater amounts of insulin administered. They had been as healthy as normal dogs up to the time of sacrifice, and had a very good appetite. That is to say, with the exception of heavy insulin-deficiency, they did not appear to be in a morbid condition. This is a state very much different from that of the totally pancreatectomized dogs in which the blood sugar level was poorly regulated.

In the insulin test in which 0.2 units of insulin were intravenously injected per kg in body weight, the blood sugar curve indicated rather mild drops and rises in Sandmeyer dog as compared with normal dog, but the tendency of recovery of the blood sugar level once dropped, was greater, when compared with totally pancreatectomized dog as shown in Fig. 4.

Fig. 4 Changes of the Blood Sugar Level (Intravenous Injection of 0.2 u/kg of Insulin).



N : Normal dog
S : Sandmeyer dog
T : Totally pancreatectomized dog
The blood sugar level before test is represented as 100.

The weights of the pituitaries and the distribution of the glandular cells in Sandmeyer dogs were given in Table 3. The percentages of the chromophil cells indicated an increase when compared with those of totally pancreatectomized dogs reported by HASEGAWA, which were 21.3% for the I type, 2.0% for the II type (HASEGAWA's II and III types),

and 76.7% for the III type (HASEGAWA's IV type). These values were distributed in the intermediate region lying between the values shown by normal dogs and by totally pancreatectomized dogs.

Table 3 Distribution of Anterior Cells in Sandmeyer Dogs.

Dog No.	Sex	Body weight kg		Pituitary weight mg	Percentage of cell types			Survival time weeks
		at the last operation	When sacrificed		Type I	Type II	Type III	
10	Male	10.6	12.3	80	54.7	2.4	42.9	34
21	Female	6.6	8.0	70	33.6	8.2	58.2	14
22	Female	11.3	12.0	70	42.2	7.6	50.1	12
23	Female	8.2	7.3	60	44.5	3.0	52.5	12
24	Male	12.2	12.6	70	41.1	4.2	54.7	12
26	Male	9.6	10.8	60	38.8	3.6	57.6	18
28	Male	12.2	13.0	90	30.5	1.2	68.3	9
29	Female	10.7	11.8	90	28.9	4.1	67.0	8
31	Female	6.4	6.8	40	31.8	6.5	54.7	14

With regard to the glandular cells of the anterior hypophysis, there were cases such as Nos. 10, 22, and 23, in which histological changes were not noted as compared with the control group. However, in Nos. 26, 31, 21, 28, etc., the pycnotic nuclei were observed in somewhat greater number in the I-type cells, while in the II-type cells, the appearance of pycnotic nuclei and of microfied granules was noted with the decrease in number of the latter. As to their attitude towards staining, many cells which were considered to be the transitional type from the β-cell to δ-cell were witnessed. A few atrophic cells were noted in the III-type cells, but such changes were slight in general.

The development of diabetes in dog No. 27 took a somewhat unusal course.

Hence, special mention will be made below. In this dog, the remnant of the pancreas communicating with the main duct was estimated to be 1.0 g at the time of the first operation. Three days after the operation and afterward, the excretion of glycosuria was seen, and the administration of insulin was required. The daily dose of insulin in this dog was 10～40 units, which amount was smaller than that in typical Sandmeyer dogs, and was rather closer to the amount of insulin administered to totally pancreatectomized dogs as mentioned by DRAGSTEDT and others. Moreover, even in such units, it frequently suffered from insulin shock, and barely relieved by glucose injection. The loss of body weight was also serious, and when it was sacrificed, it weighed only one half of the original weight.

That is to say, in dogs whose pancreas was retained only in a very small amount around the main pancreatic duct, there would arise a heavy loss in body weight even when insulin was administered, and on the other hand, the remnant of the pancreas gradually shrank, approaching to the state of totally pancreatectomized dogs. As shown in Fig. 5, the control of the blood sugar level was considerably disturbed, and the dose of insulin was found to be resembled to that of a totally pancreatectomized dogs.

Fig. 5 Amount of Insulin administered and that of Urine Sugar in Dog No. 27.

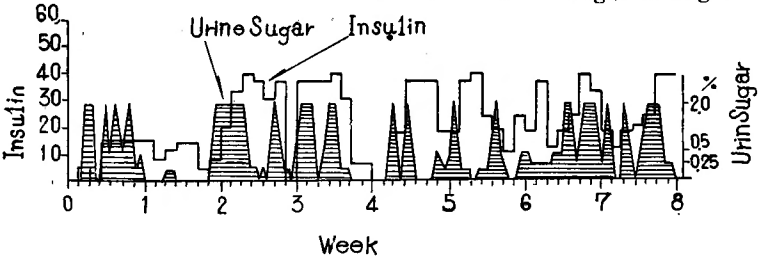


Table 4 Distribution of Anterior Pituitary Cells in Dog No. 27.

Dog No.	Sex	Body weight kg		Pituitary weight mg	Percentage of cell types			Survival time weeks
		at the operation	when sacrificed		Type I	Type II	Type III	
27	Female	8.6	4.3	50	25.5	3.4	71.1	8

Cytologically, the nuclei were found to be pycnotic in respective types. Besides, there were many cells with faintly stained granules, indicating hypofunction of the anterior pituitary lobe.

In this case, the distribution of glandular cells of the anterior hypophysis approached to that in HASEGAWA's totally pancreatectomized dogs, as showed in Table 4. Compared with the typical Sandmeyer dogs (refer to Table 3), the percentages of chromophil cells indicated a decrease.

DISCUSSION

1) According to HAMANO, to say nothing of the instances where the remnant of the pancreas was one third or one half, even when as little as about one fourth of the original size was left, diabetes did not necessarily occur, but a tendency to decrease in body weight was noted. This may mainly be due to hypofunction of digestion and absorption.

ALLEN stated that: When one eighth of the pancreas is left, in most cases, the diabetic condition is only transient, although permanent diabetes may sometimes ensue. In the case of one ninth being left, permanent diabetes is commonly obtained, and in the case of one tenth, diabetes is produced constantly in every experimental dog.

However, it is rather difficult to settle the amount of the pancreas to be extirpated definitely which is sure to produce permanent diabetes, since it is considered that the factors of heredity and of feeding environments may participate in this problem. In order to obtain Sandmeyer dogs, KAWAMURA made a partial resection of the pancreas two times successively at the interval of about two months. From my experience in this study, it was observed that when the major resection of the pancreas was done for one time, emaciation was apt to be developed instead of being accompanied by diabetes, and also demonstrated that when partial pancreatectomy was done in 2 or 3 stages, the total amount of the resected pancreas amounting to that in major resection, it was found comparatively easier to obtain permanent diabetes.

2) It has been well konwn that the anterior lobe of the hypophysis relates to the metabolism of sugar, and since various hormones of the anterior hypophysis have recently been isolated, their biological significance has much been discussed.

At present, amoung various pituitary hormones, six different kinds have been accepted of their presence independently, namely, GH, LTH, ACTH, LH, FSH, and TSH. Particularly, GH, ACTH, and TSH are considered to have close relations with sugar metabolism.

PURVES & GRIESBACH, CATCHPOLE, etc., stated that the simple protein of GH and LTH was secreted from the α-cells, and the glycoprotein such as TSH and FSH, from the β-cells in a broad sense, but no theory has yet been established as to from which cells LH or ACTH are secreted.

According to MORI, the anterior lobe of the hypophysis displays the glycotrophic action, glycostatic action, diabetogenic action, contra-insular action, pancreato-trophic action, etc.. However, as these agents are regarded as to exist mixedly with the impure extracts of the anterior lobe of the hypophysis, it has not yet known from which cells they are secreted.

However, according to the detailed studies of SEVERINGHAUS, ROMEIS and etc., the γ-cells are interpreted as static mother cells with no secreting activity, and it will be reasonable to consider that the aforementioned actions are all due to the chromophil cells.

Therefore, being connected with sugar metabolism, the percentage of the glandular cells of the anterior pituitary lobe can logically be discussed by dividing them into I and II-types which are chromophil, and the III-type which is chromophobic.

3) From this viewpoint, a schema as shown in Fig. 6 may be presented. The experimental results obtained in totally pancreatectomized dogs (HASEGAWA), in subtotally pancreatectomized dog (No. 27 of this experiment), in typical Sandmeyer dogs, and in normal dogs are shown diagrammatically in percentage of chromophil cells and arranged in such a way from the left to right in the order of description. Then a curve (A-line) gradually ascends from totally pancreatectomized dogs through the subtotally pancreatectomized one, to the Sandmeyer dogs, and then it becomes horizontal from the Sandmeyer dogs toward normal ones.

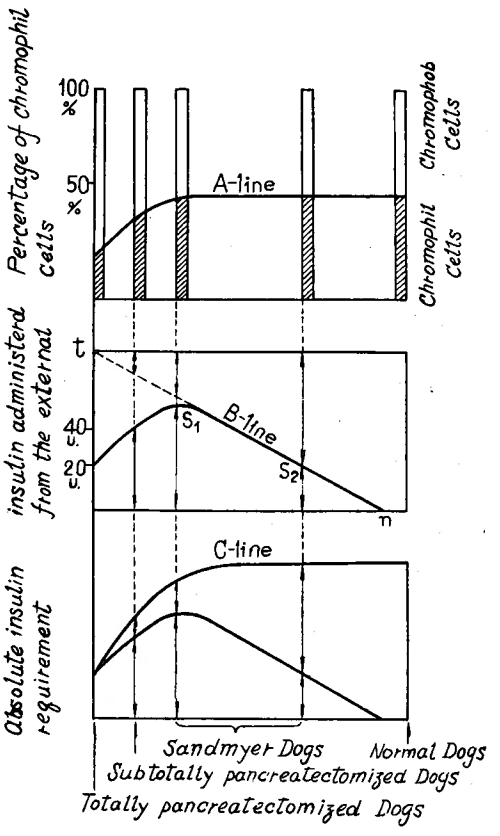
Thus, the pituitary function of Sandmeyer dogs is almost on the same level, or shows only a slight drop compared with normal dogs, and such drops in the pituitary function are heavier in sub-totally pancreatectomized dogs and heaviest in totally pancreatectomized ones.

4) Next, by arranging the insulin amounts administered respectively to DRAGSTEDT's totally pancreatectomized dogs, to sub-totally pancreatectomized dog No. 27 in this experiment, and to Sandmeyer dogs in the same manner as adopted in the preceding paragraph, B-line in Fig. 6 was obtained. In Sandmeyer dogs, they were arranged in the order from those whose pancreatic function was lowered to such a degree that it resembled closely to that of totally pancreatectomized dogs, to those which, having the comparatively well functioning pancreas, presented so healthy appearance that they looked like normal dogs.

As shown by the B-line, the insulin dose gradually increases in the oder of totally pancreatectomized dogs, sub-totally pancreatectomized, and Sandmeyer dogs. But in Sandmeyer dogs, insulin requirment tends to decrease as the remnant of the pancreas becomes greater.

When diabetes is produced by partial pancreatectomy it is commonly considered that the insulin requirement will be smaller in proportion as the remnant of pancreas is greater. In the present experiment, likewise, in the case of partially pancreatectomized dogs, a tendency was observed that the more the residual pancreatic function was preserved in a given case, the smaller the insulin requirement would be. However, when the remnant of pancreas was excessively small or naught, the insulin requirement of those animals was found to be smaller as shown in this figure.

Fig. 6



5) In Fig. 6, by extending the B-line connecting S_1 and S_2, the point where the extended line meets the horizontal-axis is set as "n", and the point where the line intersects the perpendicular axis as "t". Then a straight line is drawn from "t" in parallel with the horizontal-axis. The various heights from the line t-n to this straight line, represent the quantities of endocrinal insulin, and the heights from the horizontal axis to the B-line, the quantities of insulin administered from the external. When the total mount of the external insulin and that of internal insulin secreted from the remnant of the pancreas is termed as "the absolute insulin requirement", the relationship between this absolute insulin requirement and the amount of the remaining pancreas will be indicated by the C-line which draws a curve showing a gradual ascent from totally pancreatectomized dogs, through sub-totally pancreatectomized dogs, to Sandmeyer dogs, and then, draws a horizontal line from Sandmeyer dogs to normal dogs.

6) Between the A-line and the C-line in Fig. 6, a paralleled relationship is found with much probability. In other words, the values in percentage of chromophil cells of the anterior lobe of the hypophysis in diabetic dogs caused by pancreatectomy are closely related to the absolute insulin requirement of the animals.

7) From the results of the insulin tests in the present studies, it was demonstrated that the tendency to recover the blood sugar level is not marked in totally pancreatectomized dogs, whereas in Sandmeyer dogs, this tendency is almost on the

same level as in normal dogs. This is an interesting finding in relation to the abovementioned function of the anterior pituitary lobe.

CONCLUSION

With a view to ascertaining the difference in the insulin requirement between totally pancreatectomized dogs and Sandmeyer dogs, histological changes in the anterior pituitary lobe were investigated qualitatively and quantitatively.

1) Sandmeyer dogs could be obtained more easily by partial pancreatectomy performed in 2 or 3 stages at an interval of 1～2 months, compared with the major resection wherein a large portion of the pancreas was extirpated at a time. It is rather difficult to settle the amount of the pancreas to be resected which is sure to produce diabetes.

2) In Sandmeyer dogs, by the administration of insulin in a sufficient amount, the dogs were always as healthy as normal dogs, having a good appetite. They did not look like in a morbid state except heavy insulin-deficiency.

The tendency of recovery from a drop in the blood sugar level caused by the insulin injection, was marked as compared with totally pancreatectomized dogs.

3) The cytological changes and the percentages of the distribution of glandular cells of the anterior pituitaries in Sandmeyer dogs ranged from those in normal dogs to those in totally pancreatectomized dogs, and in some of them were not so conspicuous compared with normal dogs. However, in an case in which the removal of the pancreas was too much excessive, the development of diabetes and the amount of the insulin to be administered resembled to those in totally pancreatectomized dogs. The glandular cells were atrophic, and the value in percentage of the chromophil cells showed a heavy decrease.

4) Since opinions are not yet settled in unanimity concerning endocrinocytology of the anterior lobe of the hypophysis, the cells in the anterior lobe were grossly classified into chromophil cells and chromophobic ones. After discussing the values in percentages of these cells after the removal of the pancreas in various degrees, I proposed a schema showing a relationship between the insulin requirement and the amount of the pancreas removed. In this schema, the concept of the absolute insulin requirement is being introduced. This is the sum total of the amount of insulin considered to be secreted from the remnant of the pancreas of the diabetic dogs caused by the pancreatectomy and the amount of insulin required to be externally compensated. It is explained by the schema that the percentage of the chromophil cells of the anterior pituitaries of these animals is unrelated to the insulin amount required to be externally compensated, but is very closely related to the absolute insulin requirement.

In Sandmeyer dogs, in spite that the function of the hypophysis is as high as normal dogs, the residual functin of the pancreas is low. Thus, it is considered to have partially explained that a large amount of insulin will have to be externally compensated.

Acknowledgment

In conclusion, the author wishes to express his profound gratitude to Prof, Dr. C. Araki, and

Subprof. Dr. I. HONJO for their thoroughgoing guidance throughout the present research.

REFERENCES

1) Allen, F. M.: Studies Concerning Glycosuria and Diabetes. Chp. **X**, 461, 1913.
2) Catchpole, H. R.: Distribution of Glyco-protein Hormones in the Anterior Pituitary Gland of the Rat. J. Klin. Endocrinology, **6**, 218, 1949.
3) Dragstedt, L. R.: Extensive Insulin Tolerance in Diabetic Dogs. Proc. Soc. Exp. Biol. & Med., **54**, 292, 1943.
4) Engel, F. L., Viau, A., Coggins, W., and & Lynn, W. S.: Diabetogenic Effect of Growth Hormone in the Intact Force-Fed Adrenocorticotrophin Treated Rat. Endocrinology, **50**, 100, 1952.
5) Goldberg, R. C., & Chaikoff, I. L.: On the Occurrence of Six Cell Types in the Dog Anterior Pituitary. Anat. Rec., **112**, 265, 1952.
6) Halmi, N. S.: Two Types of Basophils in the Anterior Pituitary of the Rat and their Cytophysiological Significance. Endocrinology, **47**, 289, 1950.
7) Hamano, K.: Digestive and Absorptive Function of Gastrointestinal Tract after Various Operations of the Pancreas, Especially Total Pancreatectomy. Arch. Jap. Chir., **22**, 500, 1953.
8) Hasegawa, M.: Histologic Changes of the Anterior Hypophysis after Total Pancreatectomy, Experiment in Dogs. Arch. Jap. Chir., **24**, 154, 1955.
9) Houssay, B. A., & Biasotti, A.: The Hyophysis, Carbohydrate Matabolisum and Diabetes. Endocrinology, **15**, 511, 1931.
10) Inouye, T.: Histological Studies on the Distribution and Changes of Epithelial Cells of Adenohypophysis. Report I. A New Method for Calculating Epithelial Cells of Rat Adenohypophysis. Jap. Arch. of Internal Med., **3**, 908, 1956.
11) Kawamura, K.: The Blood Sugar Level and the Dose of Insulin Required after Total Pancreatectomy (the Sensitivity to Insulin). Arch. Jap. Chir., **23**, 578, 1954.
12) Long, C. N. H., and Lukens, F. D. W.: The Effect of Adrenalectomy and Hypophysectomy upon Experimental Diabetes in the Cat. J. Exp. Med., **63**, 465, 1936.
13) v. Mering, J., & Minkowski, O.: Diabetes mellitus nach Pancreasexstirpation. Arch. exp. Path. u. Pharm., **26**, 371, 1889.
14) Milman, A. E., de Moor, P., and Lukens, F. K. W.: Relation of Purified Pituitary GH and Insulin in Regulation of Nitrogen Balance. Am. J. Physiol., **116**, 354, 1951.
15) Mori, S.: A Texbook of Endocrinology Vol. 1, 104. Nanzando Tokyo, 1955.
16) Pflüger, E.: Untersuchungen über den Pancreasdiabetes. Pflüger's Arch., **118**, 26, 5, 1907.
17) Purves, H. D. & Griesbach, W. E.: Functional Differentiation in the Acidphil Cells and Gonadotrophic Cells of the Rat Pituitary. Proc. Unv. of Otags Med. School, **30**, 27, 1952.
18) Rasmussen, A., and Herrick, R.: A Method for the Volumetric Study of the Human Hypophysis Cerebri with Illustrative Results. Proc. Soc. Exper. Biol. & Med., **19**, 416, 1922.
19) de Renzi, E., and Reale, E.: Ueber den Diabetes mellitus nach Exstirpation des Pancreas. Berl. Klin. Wochenschr., **29**, 560, 1892.
20) Rockey, E. W.: Total Pancreatectomy for Carcinoma. Ann. Surg., **118**, 603, 1943.
21) Romeis, B.: Hypophyse. Handbuch der Mikrosk. Anat. des Menschen. Herausgeg. v. Willhelm v. Möllendorff, 6 Bd. 3 Teil.
22) Sandmeyer, W.: Ueber die Folgen der partiellen Pancreasexstirpation beim Hund. Zt schr. f. Biol., **31**, 12, 1895.
23) Scow, R. O.: Effect of Growth Hormone on Muscle and Skin Collagen in Neonatal Thyroidectomized Rats. Endocrinology, **49**, 641, 1951.
24) Severinghaus, A. E.: A Cytological Study of the Anterior Pituitary Apparats and Cell Relationship. Anat. Record., **57**, 149, 1933.
25) Young, F. G.: Permanent Experimental Diabetes Produced by Pituitary (Anterior Lobe) Injections. Lancet, **2**, 372, 1937.

Fig. 7 The middle part of the anterior pituitary lobe of the normal dog (No. 37).

The I-type cells (a) are sharply outlined, and the granules are deeply stained with azocarmin S. The II-type cells (b) are somewhat larger, being granular in their form. In the III-type cells (c), cytoplasms are indistinct and light grayish.
(Kressazan stain × 700)

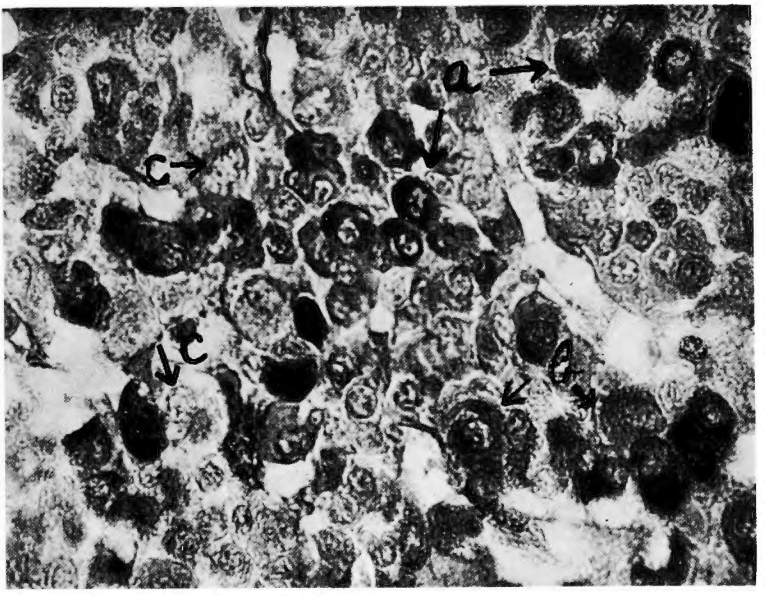


Fig. 8 The middle part of the anterior pituitary lobe of Sandmeyer dog (No. 31).

In the I-type cells, many atrophic and pycnotic cells (a_1) are seen, and the appearance of the agranular type cells (a_2) are also noted. Typical II-type cells are not to be seen. a=Typical I-type cells. (Kresazan stain × 700)

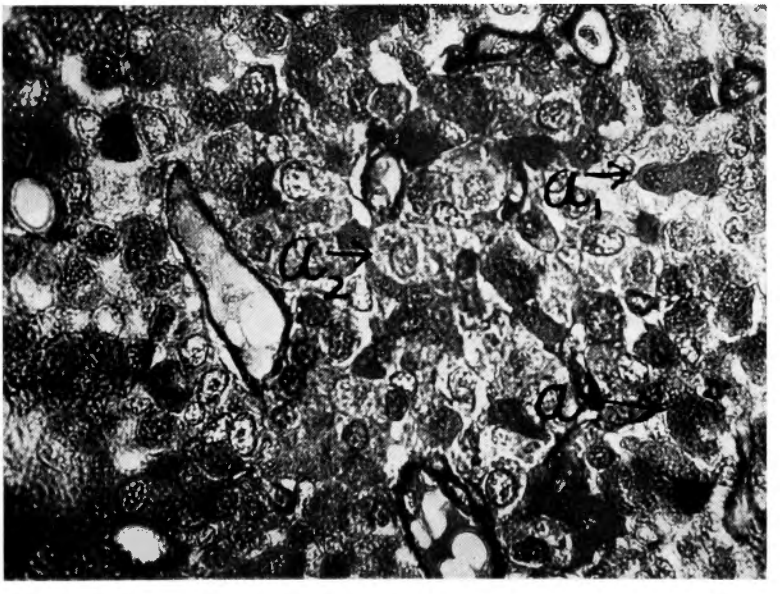
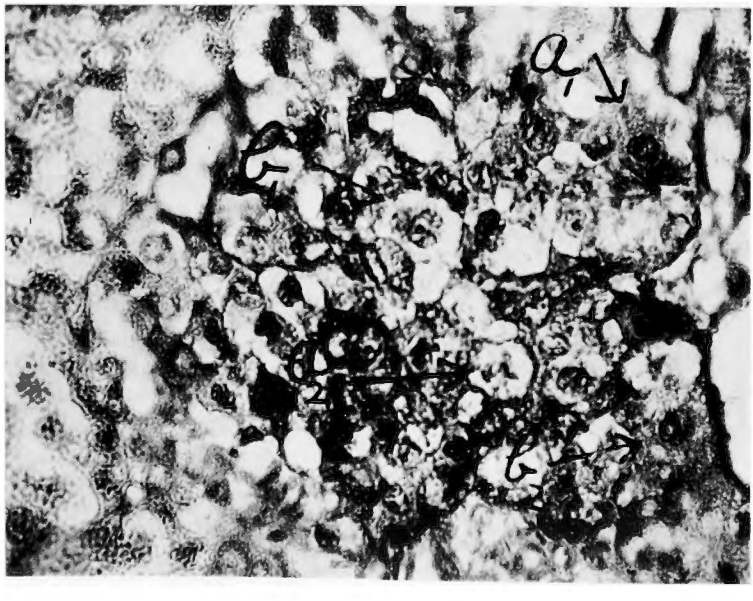


Fig. 9 The anterior pituitary lobe of Sandmeyer dog (No. 26).

The I-type cells are somewhat atrophic (a). In the II-type cells, the presence of β-δgranules are distinctly observed. The cytoplasmas are larger in size, and the granules are rough and few in number, assuming the so-called agranular form (b). (Kresazan stain × 700).

Fig. 10 The anterior pituitary lobe of dog No. 27.

The chromophil cells are generally few. The I-type cells are pycnotic (a_1), and karyolytic(a_2). Among the II-type cells, there appear those with a small number of granules (b_1) and those which are pycnotic having indistinct granules in the cytoplasms (b_2).
(PAS-azan stain × 700).



和 文 抄 録

Sandmeyer 犬における下垂体前葉の組織学的研究

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膵全切除後の糖尿病ではインシュリンの投与量は重症の内科的糖尿病に較べて非常に少ない．之に反して膵を部分切除して重症糖尿病を発症した場合は，インシュリンの投与量が多く，この様な病型はSandmeyer diabetes といわれる．この残存膵機能が保持されている Sandmeyer 犬の方が却つてインシュリンの必要量が多いという事実には，消化吸収力の差異以外に種々の内分泌臓器，特に下垂体前葉が関与しているものと考えられるので，膵全剔犬と Sandmeyer 犬のインシュリン必要量の差異を窺う目的で， Sandmeyer 犬について，その下垂体前葉の態度を組織学的に検討した．

Kresazan 染色を施した組織標本に就いてRasmussen Herrick 氏法の変法である井上氏の三視野法によつて各種細胞の量的変化を追求すると共に，質的変化をも併せ検索した．

下垂体前葉の分泌細胞学に就いては，現今尚，意見の一致を見ていないので，色素好性細胞と色素嫌性細胞に分けて考察し，1つの模式図を示して考案を加えた．

1) Sandmeyer 犬の下垂体前葉では，色素好性細胞の百分率は正常犬のそれに比して，殆ど同じであるか，稍低下を示した．しかし之は，先に当教室の長谷川の報告している膵全剔犬のそれに較べると非常に高い．又対照群に比して特に細胞学的変化の見られなかつたものもあるが，各型共に稍々萎縮性のものも見られた．

2) 膵切除量が過大であつた1例では，病像並びにインシュリン投与量は膵全剔犬に相似し，下垂体前葉細胞は萎縮性で，色素好性細胞の百分率の値は著しい低下を示した．

3) 模式図では absolute insulin requirement という概念を導入した．之は，膵部分切除犬で，残存膵が分泌していると考えられるインシュリン量と，外来として与えるインシュリン量の和で，当該膵部分切除犬の要求している全体としてのインシュリン量という意味である．

膵部分切除した犬で，インシュリンを適度に与えた場合，その動物の下垂体前葉色素好性細胞の百分率の値は，インシュリン投与量との間には必ずしも相関々係は認められないが，absolute insulin requirement との間には平行的な関係のあることを，模式図によつて示した．

Sandmeyer 犬では下垂体の機能は比較的よく保持され，インシュリン要求量も多いに拘らず，分泌しているインシュリン量は少ない．従つて Sandmeyer 犬では多量のインシュリンを投与しなければならないものと考える．

又膵切除量が過大であつた1例や，膵全剔犬の如くインシュリン必要量の少ない場合も本模式図によつて説明し得る．