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On Adrenalinaemia resulting from Central Glycosuria, as studied by the Quantitative Change of Glycogen in the Milk-spots.

By **Dr. Yukio Hamazaki.**

From the Pathological Department of Okayama Medical College. (Director: Prof. Oto Tamura)

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Introduction.

Whether or not central glycosuria is caused by adrenalinaemia similarly to the peripheral one, is a very important question which has been taken up by many investigators.

For this problem André Mayer's work (1906) that the diabetic puncture made after the removal of both the adrenals does not cause glycosuria, has been considered as the experimentum crucis. However, this inference may not be correct, since his result is nothing but a proof that the effect of diabetic puncture does not reach directly the liver,

but indirectly by way of the supra-renal glands. Therefore, it becomes very desirable to determine how this stimulation reaches the liver from the glands. In the preceding paper entitled "Studies on glycogen of the milk-spots in the omentum" I reported in a preliminary way on the changes of the milk-spots in the cases of piqûre and injection of diuretin, adrenalin and phloridzin. And in the present I shall deal with the same subject in some detail.

Glycogen in the milk-spots of the healthy adult rabbit was fully described in the preceding paper. But by way of introduction I may repeat the statement here. In 60% of the healthy adult rabbits glycogen is present in the milk-spots in the following proportion; $(++):(+):(\pm):(-) = 1:1:1:2$. In the omentum glycogen is always deposited only in the milk-spots, and it is mostly contained in the histiocytic cells there and in small quantity in the mesothelial cells.

I. Methods.

The rabbits were fed with "Tôfukasu", residual of soya-bean cheese. Tissues from the rabbits were passed through graded alcohols up to absolute and were examined either as stretched specimens or as celloidin-sections. Best's potassium carmine method was mostly used for glycogen-stain and Langhan's iodine method and saliva-reaction were also made use of. Blood-sugar was determined by Kasamatsu and Hattori's method. The blood for sugar-test was obtained from the auricular vein, keeping the animal in natural condition without being fastened. Glycosuria was tested by Nylander's and Trommel's methods.

II. Central glycosuria.

1. Piqûre.

In 1854 and 1855 Cl. Bernard discovered that glycosuria is produced by means of puncture on the median line of the floor of the fourth ventricle bounded by the lines, one connecting the origins of both the auditory nerves and the other connecting the origins of both the vaguses and he designated this region "sugar-centre". According to Bernard and Eckhard, the stimulation produced by the puncture goes downwards along the spinal to the first thoracic vertebra and reaches the liver by way of the truncus sympathicus and the n. splanchnicus, thus causing the transformation of glycogen into sugar in the liver. Blum (1901) observed that the injection of the extract of the supra-renal glands causes a glycosuria and basing upon this fact he conjectured that the glycosuria due to piqûre may stand in an intimate relation to the function of the suprarenals.

Thereafter, Blum's view was supported by Mayer's piqûre experiments made after the extirpation of the suprarenals.

Experiments:—

Piqûre was performed according to Eckhard's method, that is, after the removal of the membrana atlanto-occipitalis the puncture was made. The examination was made two, four, six, eight, twelve and 24 hours after from the operation. Tests of hyperglycemia and glycosuria were made twice, i. e., before injection and at the time of sacrifice.

The results are shown in the following tables I and II.

Table I. Diabetic puncture. Series I.

No. of case and sex.			25 ♂	26 ♂	27 ♂	28 ♂	29 ♂	30 ♂
Body-weight (grm)			1580	1640	1760	1820	1630	1590
Sacrifice-time (hour)			2	4	6	8	12	24
Milk-spots	Hist. cell	B. p. g.	++	++	±	++	−	−
		L. p. g.	+	+	−	+	−	−
	Mesothelial cell	B. p. g.	±	+	−	+	−	−
		L. p. g.	−	−	−	−	−	−
	Polymorph. leucocyte	Presence	−	−	−	−	−	±
		B. p. g.						±
Mesentery	B. p. g.		−	−	−	−	−	−
	L. p. g.		−	−	−	−	−	−
Blood-sugar (%)	before injection		0.103	0.089	0.095	0 091	0.099	0.093
	before sacrifice		0.147	0.160	0.185	0.200	0.105	0.108
Glycosuria	before injection		−		−	−	−	−
	before sacrifice		+	+	+	+	±	−
Liver-glycogen.			±	+	+	++	+++	+++

Note: Hist. cell = Histiocytic cell. B. p. g. = Best's positive granules.
L. p. g. = Langhan's positive granules.
The hyperglycaemia and glycosuria in the Tables I, II, III and VI were proved by Dr. Fujihara.

Series I.

The Best's positive granules are contained in the histiocytic cells of the milk-spots abundantly in Cases 25, 26 and 28, sparcely in Case 27, none in Cases 29 and 30.

Blood-sugar: it increases from two to eight hours after the puncture and returns to the normal after twelve hours.

Glycosuria: positive from two to eight hours after the puncture, only trace twelve hours after.

Liver-glycogen: in traces two hours after the puncture, from four to eight hours gradually increases, twelve and 24 hours, nearly normal.

Series II.

In Cases 31 and 33 the Best's positive granules can be found numerously, in Case 34 in medium quantity, in Case 36 in trace and in Cases 32 and 35 none.

Blood-sugar: increases from two to eight hours after the puncture and it returns to the normal after 24 hours.

Glycosuria: in all cases positive.

Liver-glycogen: from two to eight hours after the puncture in trace, twelve and 24 hours somewhat abundant.

Table II. Diabetic puncture. Series II.

No. of case and sex.			31 ♂	32 ♂	33 ♂	34 ♂	35 ♂	36 ♂
Body-weight (grm)			1750	1790	1680	1670	1810	1560
Sacrifice-time (hour)			2	4	6	8	12	24
Milk-spots	Hist. cell	B. p. g.	++	−	++	+	−	±
		L. p. g.	+	−	+	±	−	−
	Mesothelial cell	B. p. g.	±	−	+	+	−	−
		L. p. g.	−	−	−	−	−	−
	Polymorph. leucocyte	Presence	±	−	−	−	+	−
		B. p. g.	−				+	
Mesentery		B. p. g.	−	−	−	−	−	−
		L. p. g.	−	−	−	−	−	−
Blood-sugar (%)		before injection	0.089	0.095	0.104	0.096	0.101	0.087
		before sacrifice	0.159	0.165	0.191	0.135	0.142	0.115
Glycosuria		before injection	−	−	−	−	−	−
		before sacrifice	+	+	+	+	+	+
Liver-glycogen			±	±	±	±	++	++

In the hyperglycemia produced by means of puncture glycogen of the milk-spots remarkably increases as compared with the normal. The above results may be shown thus; in Series I, (++):(+):(±):(−) = 3:0:1:2, in Series II, (++):(+):(±):(−) = 2:1:1:2.

2. Diuretin injection.

In 1895 Jacoby observed that the injection of the derivatives of caffein in the rabbit previously fed with food rich in carbohydrate causes a glycosuria and he termed it "Nierendiabetes". Richter, however, opposed Jacoby's view, recognizing the occurence of hyperglycemia and diminution of liver-glycogen in the case of diuretin-glycosuria. He thought that it is the so-called liver-glycosuria due to the increased reduction of liver-glycogen. Later, Rose emphasized from his experiment that hyperglycemia appears prior to glycosuria.

Experiment:—

10 c.c. of 6% diuretin in normal saline solution was subcutaneously injected per kilogram of body-weight and examined at intervals of one, two, three, four, five and seven hours. Hyperglycemia and glycosuria were tested twice; once just before injection and the other time when sacrificed.

The results are shown in the following table.

Table III. Diuretin-injection.

No. of case and sex.			19 ♂	20 ♂	21 ♂	22 ♂	23 ♂	24 ♂
Body-weight (grm)			1350	1280	1450	1720	1650	1530
Sacrifice-time (hour)			1	2	3	4	5	7
Milk-spots	Hist. cell	B. p. g.	±	+	+	++	+	−
		L. p. g.	−	−	±	+	±	−
	Mesothelial cell	B. p. g.	−	±	±	+	−	−
		L. p. g.	−	−	−	−	−	−
	Polymorph. leucocyte	Presence	−	++	++	−	−	−
		B. p. g.		−	++			
Mesentery		B. p. g.	−	−	−	−	−	−
		L. p. g.	−	−	−	−	−	−
Blood-sugar (%)		before injection	0.097	0.106	0.103	0.091	0.093	0.086
		before sacrifice	0.108	0.176	0.201	0.156	0.133	0.121
Glycosuria		before injection	−	−	−	−	−	−
		before sacrifice	−	+	+	+	+	±
Liver-glycogen			+	±	++	+	+	++

The Best's positive granules of the milk-spots are present abundantly in Case 22, moderately in Cases 20, 21 and 23, in trace in Case 19 and none in Case 24.

Blood-sugar: it reaches the maximum three hours after the injection and gradually decreases until it nearly returns to normal after seven hours.

Glycosuria: from two to five hours after the injection, positive, seven hours after, in trace.

Liver-glycogen: only in trace in Case 20, somewhat highly diminishes in Cases 19, 22 and 23 and moderately in Cases 21 and 24.

Judging from the above experiment, it may be stated that in hyperglycemia due to diuretin-injection the glycogen in the milk-spots decidedly increases. The proportion may be shown in this way; $(++):(+):(\pm):(-) = 1:3:1:1$.

III. Peripheral glycosuria.

In 1901 Blum subcutaneously injected the extract of the suprarenals in the dog and rabbit and succeeded in causing an experimental glycosuria. Later, Herter and Richards et al. proved that the effective substance of the suprarenal glands is the adrenalin. Zülzer, Metzger et al. recognized that glycosuria is preceded by hyperglycemia.

Experiment:—

Series I.

0.4 c.c. of adrenalin chloride 1:1000 was subcutaneously injected with the ratio of per kilogram of body-weight and examined after one, two, three, four, five and seven hours. Hyperglycemia and glycosuria were tested twice, i. e., just before injection and at the time of sacrifice.

The following table shows the results.

Table IV. Adrenalin-injection. Series I.

No. of case and sex.			43 ♂	44 ♂	45 ♂	46 ♂	47 ♂	48 ♂
Body-weight (grm)			1320	1790	1815	1960	1605	1750
Sacrifice-time (hour)			1	2	3	4	5	7
Milk-spots	Hist. cell	B. p. g.	−	±	−	−	−	±
		L. p. g.	−	−	−	−	−	−
	Mesothelial cell	B. p. g.	−	−	−	−	−	−
		L. p. g.	−	−	−	−	−	−
	Polymorph. leucocyte	Presence	±	−	+	±	−	±
		B. p. g.	±		+	±		±
Mesentery		B. p. g.	−	−	−	−	−	−
		L. p. g.	−	−	−	−	−	−
Blood-sugar (%)		before injection	0.104	0.110	0.115	0.098	0.102	0.097
		before sacrifice	0.275	0.306	0.304	0.326	0.314	0.222
Glycosuria		before injection	−	−	−	−	−	−
		before sacrifice	+	+	+	+	+	+
Liver-glycogen			++	+	+	±	++	++

The Best's positive granules can be detected sparcely in Cases 44 and 48, none in Cases 43, 45, 46 and 47.

Blood-sugar: it increases remarkably one hour after the injection and reaches the maximum after four hours. After seven hours, still the hyperglycemia remains in medium degree.

Glycosuria: in all cases, positive.

Liver-glycogen: in Cases 43, 47 and 48 diminishes moderately, in Cases 44 and 45 more decreases and in Case 46 still more.

Series II.

Table V. Adrenalin-injection. Series II.

No. of case and sex.			49 ♂	50 ♂	51 ♂	52 ♂	53 ♂	54 ♂
Body-weight (grm)			1600	1720	1485	1720	1476	1520
Sacrifice-time (hour)			1	2	3	4	5	7
Milk-spots	Hist. cell	B. p. g.	−	−	−	−	−	−
		L. p. g.	−	−	−	−	−	−
	Mesothelial cell	B. p. g.	−	−	−	−	−	−
		L. p. g.	−	−	−	−	−	−
	Polymorph. leucocyte	Presence	−	−	±	−	−	−
		B. p. g.			±			
Mesentery		B. p. g.	−	−	−	−	−	−
		L. p. g.	−	−	−	−	−	−
Blood-sugar (%)		before injection	0.089	0.108	0.099	0 116	0.105	0.097
		before sacrifice	0.253	0.368	0.406	0.313	0.362	0.223
Glycosuria		before injection	−	−	−	−	−	−
		before sacrifice	+	+	+	+	+	+
Liver-glycogen			±	±	±	+	+	+

The quantity of the adrenalin injected was incraesed to 0.8 c.c. per kilogram of body-weight.

In all cases no Best's positive granules are present.

Blood-sugar: increases markedly one hour after the injection and reaches the maximum three hours after. After seven hours, hyperglycemia still remains in medium degree.

Glycosuria: in all cases positive.

Liver-glycogen: in Cases 52, 53 and 54 remarkably diminishes and in Cases 49, 50 and 51 still more.

From the above experiment one may observe that in the hyperglycemia due to adrenalin-injection glycogen in the milk-spots very much decreases or totally disappeares, namely; $(++):(+):(\pm):(-) = 0:0:2:4$, in Series I and $(++):(+):(\pm):(-) = 0:0:0:6$, in Series II.

IV. Renal glycosuria.

v. Mering reported that in phloridzin-administration in the dog glycosuria appeared remarkably, but hyperglycemia did not. He claimed this to be a case of renal glycosuria. However, Pavy, Biedl and Kolisch recognized hyperglycemia in phloridzin-glycosuria and opposed Mering's view. In phloridzin-glycosuria, Minkowski found that the sugar-contents of the blood is not augmented, but on the contrary, it is frequently diminished. Later, Erlandsen, Czyhalz and Schlesinger, Lewandowsky et al. agreed with Mering's view.

Experiment:—

2% phloridzin-suspension in olive-oil was subcutaneously injected with the dose of 10 c.c. per kilogram of the body-weight and examined after one, two, three, four, five and seven hours. Hyperglycemia and glycosuria were tested twice, i. e., just before injection and at the time of sacrifice.

The results are shown in Table VI.

The Best's positive granules are found numerously in Case 41, moderately in Case 42, sparcely in Cases 38, 40 and none in Cases 37, 39.

Blood-sugar: no changes by time. It ranges from 0.104 to 0.089, on an average 0.097, before the injection and from 0.102 to 0.093, on an average 0.095 just before sacrificed.

Glycosuria: in all cases positive.

Liver-glycogen: a mere trace in Cases 39, 41 and in the other cases, nearly normal.

Form the above results one can see that glycogen-contents of the milk-spots has no influence on the renal-glycosuria caused by phloridzin-injection. The proportion in these cases, $(++):(+):(\pm):(-) = 1:1:2:2$, is nearly similar to the normal, $(++):(+):(\pm):(-) = 1:1:1:2$.

Table VI. Phlaridzin-injection.

No. of case and sex.			37 ♂	38 ♂	39 ♂	40 ♂	41 ♂	42 ♂
Body-weight (grm)			1350	1260	1410	1290	1320	1320
Sacrifice-time (hour)			1	2	3	4	5	7
Milk-spots	Hist. cell	B. p. g.	−	±	−	±	++	+
		L. p. g.	−	−	−	±	+	±
	Mesothelial cell	B. p. g.	−	±	−	−	+	±
		L. p. g.	−	−	−	−	−	−
	Polymorph. leucocyte	Presence	−	−	−	−	−	−
		B. p. g.						
Mesentery		B. p. g.	−	−	−	−	−	−
		L. p. g.	−	−	−	−	−	−
Blood-sugar (%)		before injection	0.101	0.089	0.096	0.092	0.098	0.104
		before sacrifice	0.095	0.095	0.102	0.093	0.094	0.090
Glycosuria		before injection	−	−	−	−	−	−
		before sacrifice	+	+	+	+	+	+
Liver-glycogen			++	+++	±	+++	±	+++

V. Diuretin-injection followed by adrenalin.

Glycogen in the milk-spots evidently increases at central hyperglycemia, while it highly diminishes or totally disappeares at peripheral hyperglycemia. So it is of interest to see of the increased glycogen in the milk-spots as the results of diuretin-injection is in some way influenced by adrenalin.

Experiment:—

6% diuretin in normal saline solution was subcutaneously injected in such proportion as 10 c.c. per kilogram of body-weight and four hours later the animal was sacrificed. $\frac{1}{4}$, $\frac{1}{2}$, 1 and 2 hours before the time of sacrifice adrenalin chloride was subcutaneously injected in a dose of 0.4 c.c. per kilogram of body-weight. Blood-sugar and glycosuria were determined just before diuretin-, adrenalin-injection and at the time of sacrifice.

The results are shown in Table VII.

The Best's positive granules of the milk-spots can be detected in a trace in Case 66, without even a trace in Cases 67, 68 and 69, while in Case 70 (control) the granules exist abundantly.

Glycosuria: in all cases positive.

Liver-glycogen: in Case 66 slightly decreases, in Cases 67, 68 and 70 strongly decreases and in Case 69 only in a trace.

From the above results, it may be concluded that the increased glycogen-depot of the milk-spots in the case of diuretin-injection is almost entirely diminishes by adrenalin-injection.

Table VII. Diuretin-injection followed by adrenalin.

No. of case and sex.			66 ♂	67 ♂	68 ♂	69 ♂	70 ♂
Body-weight (grm)			1780	1785	2250	1890	2030
Sacrifice-time (hour)	after diuretin-inj.		4	4	4	4	4
	after adrenalin-inj.		¼	½	1	2	
Milk-spots	Hist. cell	B. p. g.	±	−	−	−	++
		L. p. g.	−	−	−	−	+
	Mesothelial cell	B. p. g.	−	−	−	−	+
		L. p. g.	−	−	−	−	±
	Polymorph. leucocyte	Presence	±	−	−	+	−
		L. p. g.	−			±	
Mesentery	B. p. g.		−	−	−	−	−
	L. p. g.		−	−	−	−	−
Blood-sugar (%)	before diuretin-inj.		0.121	0.089	0.098	0.109	0.117
	before adrenalin-inj.		0.290	0.171	0.260	0.184	
	before sacrifice		0.298	0.186	0.282	0.341	0.206
Glycosuria	before diuretin-inj.		−	−	−	−	−
	before adrenalin-inj.		+	+	+	+	
	before sacrifice		+	+	+	+	+
Liver-glycogen			++	+	+	±	+

VI. Review of literature and discussion.

As Blum succeeded in producing an experimental glycosuria by the injection of the extract of the suprarenals he inferred that the glangs may be able to cause glycosuria also in vivo and that there may be an intimate relation between diabetic puncture and the suprarenals. His inference was later verified by André Mayer's experiment that the glycosuria caused by puncture does not occur after both the adrenals were extirpated. Later, Kahn and Starkenstein, Landau et al. affirmed the results of this experiment. The diuretin-hyperglycemia is also inhibited by the extirpation of both the adrenals or splanchnicotomy as formed out by Nishi. Many other cases of central hyperglycemia, such as produced by morphin-, strychinin-, chloroform-administration, stimulation of the sensory nerves etc. are also checked by the cutting of the splanchnici that are the secretory nerves of the adrenals (Pollak).

These experiments strongly supported the adrenalin-theory held by Blum et al., but at the same time one should not neglect to see how the liver-glycogen is affected by the removal of the adrenals. Schwarz, Kahn and Starkenstein, Porges et al. noticed that the liver-glycogen is strongly decreased or totally disappeared after the extirpation of both

the adrenals, whereas the fact that piqûre made after the removal of the adrenals was not successful may be due to the lack of liver-glycogen. Furthermore, in the case of the removal of adrenals the quantity of urine is usually markedly diminished. In such case, as is well known, glycosuria often does not take place, in spite of the presence of a remarkable hyperglycemia. Therefore, in the experiment of Mayer et al., it is considerable that hyperglycemia existed. Wertheimer and Battez stated that hyperglycemia due to piqûre can be demonstrated in the cat from which the adrenals have been extirpated and Mc Guigan also succeeded in producing the salt-glycosuria after the removal of the adrenals. According to Kahn and Starkenstein, the liver-glycogen of the rabbit contrary to other animals is not influenced by the removal of the adrenals, and yet no glycosuria appear by the puncture. Freund and Marchand proved, however, that the hyperglycemia not accompanied by glycosuria almost always appears by the puncture in the epinephrotomized rabbits. Reducing from this fact, they insisted that the effect caused by the piqûre does not affect the adrenals at all, but the liver directly.

It is to be noted that there are many differences between the glycosuria due to piqûre and adrenalin-glycosuria. Piqûre does not work on any starved animals (Bernard, Dock et al.), while the adrenalin-glycosuria appears in such cases (Bang). And it is considered by many that in the case of piqûre the sugar is mainly derived from the liver-glycogen while at the adrenalin-glycosuria it comes from both the liver- and muscle-glycogen. According to Pollak, by continued administration of adrenalin in the starved rabbit, the liver-glycogen is formed and muscle-glycogen deminished. Hirudin previously administered intravenously inhibits the adrenalin-glycosuria, but it has no influence on the diuretin-glycosuria (Miculicich). On narcotized animals piqûre does not work, while adrenalin does (Eckhard). Chloralhydrat represses hyperglycemia due to piqûre, but it does not act on adrenalin-glycemia (Bang).

All what have been said oppose adrenalin-theory and we are quite at a loss to why there exist such remarkable differences between the action of the mobilized adrenalin by piqûre and that of injected adrenalin. Although at first Cl. Bernard, Eckhard, Pflüger et al. considered that the action of puncture reaches directly the liver-cells via the splanchnici, a new theory was put forth basing upon Mayer's experiment, that the stimuli may pass through the adrenals. However, how the stimuli which have reached the adrenals get to the liver-cells is still an open question. One naturally takes recourse in adrenalinemia to explain this, but it has met with many objections as above-mentioned. Therefore, Nishi inferred that the adrenals and the liver may be connected with some nerves. Lately, basing upon Lichtwitz's view that adrenalin runs in the sympathic sys-

tem, Tammann punctured the rabbit after unilateral extirpation of the adrenals and cut the liver into two parts along the Lig. longitudinale hepatis and measured the quantity of glycogen contained in each half separately. He found out that in the half on the side without the adrenal, glycogen is consumed far less than in the opposite half. "Eine befriedigende Erklärung dieses Phenomen ist" he said "nur möglich unter der Annahme, dass das Adrenalin nicht in der Blutbahn, sondern im Sympathischen Nerven seinen Weg zur Leberzellen nimmt".

Whether or not the adrenalin-quantity of the blood increases by piqûre has been much discussed by many investigators. Using Ehrmann's frog-eye-reaction Waterman and Smit reported that the adrenalin-quantity of the blood is hightened by puncture. But Borberg and Lopez denied this. Kahn also proved that neither the serum of the arterial blood nor that of the venous blood showed any vasoconstrictive action in the case of puncture. Trendelenburg and Fleischhauer measured the quantity of adrenalin which is necessary to produce glycosuria by continued intravenous infusion of adrenalin and they confirmed that this amount is sufficient to highten the blood-pressure. But since neither piqûre nor diuretin-injection has any influence whatever on the blood-pressure, they declined to accept the theory that central glycosuria is attributable to adrenalinemia. Nishi reported that after diuretin-injection the blood-serum shows no effect at all on the frog's eye. By means of unilateral removal of the uppermost cervical ganglion, Negerin succeeded in giving the iris an adrenalin-sensibility on the operated side. From the animal thus operated, he obtained results that epinephrin discharged from the adrenals after puncture reaches the eye in sufficient amount to produce glycosuria. K. Shimidzu also recognized the appearance of adrenalinemia in similar experiments. However, Elliot proved that in the similar experiments mydriasis still appears in the animal without the adrenals. Carrasco-Formiguera punctured the cat with the denervated heart following Cannon's adrenalin-test and made out that tachycardia occured immediately after the piqûre. This phenomenon was inhibited by the extirpation of the adrenals or their denervation. When the abdominal cava was temporarily clamped above the lumbo-adrenal vein, the heart rate went down, and when the clamp was removed, it quickly increased. He concluded from these facts that "the piqûre produces the discharge from the adrenal glands of a product that reaches the arterial blood in sufficient amount to exert on other organs an action identical to that of adrenalin". Trendelenburg and Fleischhauer emphasized that the glycosuria due to piqûre is not the action of the hormon discharged from the adrenals, but the former lately changed his view by new experiment that immediately after piqûre the adrenalinemia takes place

which is capable of elicitting the glycosuria. With no experimental basis he made a compromise that the glycogen-mobilization by puncture induces adrenalinemia, and in addition the impulses may reach the liver-cell by way of the nerves.

Many investigators judged indirectly the quantity of adrenalin in the blood from the amount of chromaffin substance of the adrenals in the case of central glycosuria. Jarisch, Kahn, Pfeiffer et al. reported that the chromaffin substance has diminished by puncture. Negerin and Brücke, and Fujii admitted the above mentioned fact, yet at the same time they noticed that the similar phenomenon can be observed even when puncture fails to produce the glycosuria. Fujii obtained the result that when unilateral splanchnicotomy was done prior to the piqûre, the adrenal on the denervated side did not any change at all, while the chromaffin substance of the opposite gland was markedly diminished or sometimes entirely disappeared.

It should be stated, however, that the decrease of the chromaffin substance of the adrenals may take place by the increased discharge of adrenalin, and by the depressed adrenalin-formation just as well and this makes the correlation between the amount of chromaffin substance and that of adrenalin in blood very uncertain. Furthermore, this uncertainty is enhanced by the fact that brown coloring of the adrenals by bichromate-fixation can not be taken as a reliable adrenalin-reaction (Kahn, Trendelenburg, Kutschera-Aichberger et al.).

I have made some observations on the changes of chromaffin substance of the adrenals subsequent to diuretin- and adrenalin-injection. In each case the right adrenal was made transparent macroscopic preparation according to Negerin and Brücke's method and the left one into serial paraffin sections. In the case of diuretin-injection the chromaffin substance sometimes diminished as compared with the normal one. So also with the case of adrenalin-injection. No fundamental differences between diuretin- and adrenalin-injection could be made out regarding the amount of chromaffin substance.

From what has been said it will be seen that there is still a divergence of views concerning adrenalinemia by the central glycosuria. My experiments yielded the results as before mentioned that the glycogen in the milk-spots markedly increases by piqûre and diuretin-injection, while it very much decreases or entirely disappears by adrenalin-injection, and that the increased glycogen-depot of the milk-spots by diuretin-injection is evidently reduced by adrenalin-injection. These facts are naturally incompatible with the adrenalinemia-theory.

VII. Conclusions.

1. The quantity of glycogen in the milk-spots remarkably increases at central glycosuria, while it markedly decreases or entirely disappears at peripheral glycosuria. It is not influenced at all at renal glycosuria.

2. Glycogen-depot of the milk-spots increased by diuretin-injection is markedly diminished by adrenalin-injection.

3. Taking these facts into consideration, it will be said that the origin of central glycosuria may not be the same as that of adrenalin-glycosuria.

In ending, I wish to acknowledge my indebtedness to Profs. O. Tamura and H. Tanabe and also to express my gratitude to Dr. Fujihara who has kindly put valuable materials at my disposal.

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內 容 大 意

乳斑糖原質ノ消長ヨリ見タル中樞性糖尿ニ於ケル「アドレナリン」血症ノ疑義

岡山醫科大學病理學教室（主任，田村教授）

濱 崎 幸 雄

中樞性糖尿ノ Mechanismus ニ關シテハ大別スレバ三樣ノ說アリ．Bernard, Eckhard, Pflüger 氏等ハ糠中樞ヨリノ興奮ハ交感神經系ヲ經テ肝ニ直達スルモノナリト論ジ，Blum, Mayer 氏等ハ交感神經ヲ經テ副腎ニ達シ其ノ分泌亢進ヲ惹起シ「アドレナリン」血症ヲ招來スルニ因ルモノナリトナシ，Nishi, Tammann 氏等ハ副腎ト肝ハ神經ヲ以テ連絡スルモノナラント推論シ，Kahn, Trendelenburg 氏等ハ肝直達說ト副腎介在說トノ折衷說ヲ唱ヘ，各自々說ヲ高唱シテ互ニ讓ラズ．

著者ハ諸種ノ實驗的糖尿病ニ於ケル乳斑糖原質ノ消長ヲ檢セシ所，ソノ糖原量ハ中樞性糖尿症ニ於テハ著シク增加シ，末梢性糖尿症ニ於テハ之ニ反シテ甚シキ消耗乃至消失ヲ來ス．又「ヂウレチン」注射ニヨリテ增量セル糖原質ハ「アドレナリン」注射ニヨリテ著シク減少スルヲ確認セリ．

本實驗成績ハ中樞性糖尿ノ本態ヲ「アドレナリン」血症ニ歸セントスル說トハ相容レザル所，從ツテ中樞性糖尿症ト末梢性糖尿症トハソノ本態ニ於テ同一ノモノト見做スヲ得ズ．